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American Journal of Diseases of Children

VOLUME 36 DECEMBER, 1928 NUMBER 6

POSTURAL REFLEXES

IN RELATION TO THE CORRECTION OF IMPROPER BODY POSITION*

ROYAL STORRS HAYNES, M.D.

NEW YORK

Improper body position implies the lack of the use, or the incorrect use, of groups of muscles which are necessary for the maintenance of the erect attitude. The causes of this condition are many, but they will not be considered in this paper.

In the correction of improper body position, one must obtain all or several of the following: (1) inversion of the feet, (2) extension of the knee, (3) extension of the hip, (4) reduction of the lumbar lordosis, (5) extension of the dorsal spine, (6) elevation (which also means widening) of the thoracic cage, (7) straightening of the cervical spine and (8) leveling of the head.

I cannot now consider the mechanical problems concerned in these readjustments. The general problem is to bring into proper action the antigravity muscles so that the body may be erect, the vital organs may function correctly, and there may not be an unnecessary expenditure of energy. The position and the use of each part of the body must be considered in relation to all the other parts, for that which affects one part directly affects all the other parts indirectly.

Whatever method may be used to bring about these desired readjustments, it must create a voluntary control of the necessary muscles or groups of muscles. Sometimes the use of these muscles or groups of muscles is outside the consciousness of the subject. If asked to make a given corrective movement, he may be unable to do so and may declare that he is paralyzed, and yet, given a general movement which he is accustomed to make and for which, therefore, he has the necessary cortical picture, he will be able to move the "paralyzed" muscles, if they are included in this general movement, with force and facility. By repeating the movement which he is capable of making, and which brings these muscles into play, his attention may be directed to the desired muscle or group of muscles so that he becomes conscious of it, and can

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* From the Department of Pediatrics, College of Physicians and Surgeons, Columbia University.

reproduce the feeling that its contraction in the larger movement has given him. In that way, he may acquire the ability to use the muscle by itself.

In this manner, having an understanding of what combinations of muscles are necessary to achieve a correction of improper body position, one may build up in the consciousness of the subject new and correct action patterns which his will may translate into an associated muscular effort that will bring the various parts of the body into correct relation-

Fig. 1.—A boy, the correction of whose improper body position requires the obtaining of all the readjustments mentioned. The eversion of the feet cannot be seen from this aspect.

ship. Repeated conscious use of these associations will result in their becoming habitual or unconscious, so that, after a comparatively short interval, his new attitude will become the usual attitude and only with

1. I had the experience of presenting before a body of physicians, a girl, aged 11, who demonstrated at will good and poor body position. A month or two later, before a similar gathering, it was almost impossible for her to demonstrate the bad position out of which she had been trained.

difficulty and perhaps without complete success will he be able to assume his earlier and incorrect position.[1]

I have worked for a number of years on the correction of faulty position in children, using associations of muscles which seemed to me to be correct from the mechanical point of view. It is my habit to begin with the muscles which extend the body at the hip and knee.

A comparison of the attitude of human beings with that of the primates or that of the pronograde animals brings out certain essential differences in their musculature, and also points to a similarity in the necessity among all of them for effort in maintaining the body erect.

The striking difference is in the knee and hip extensors. These muscles in man have reached their greatest development in proportional strength and bulk. It is due to the strength and ability of these muscles

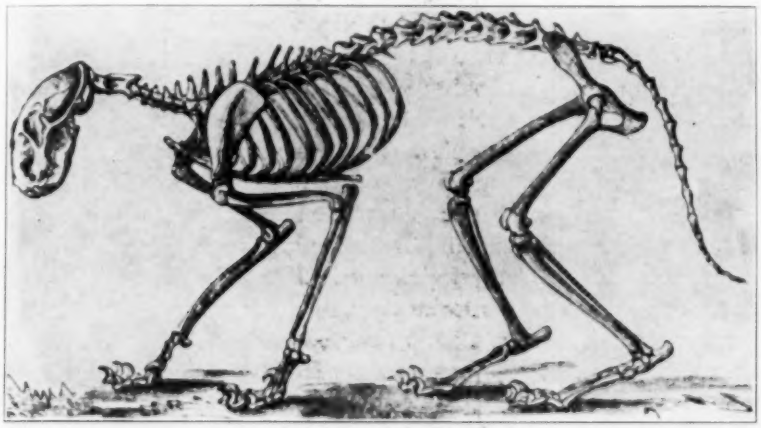

Fig. 2.—Skeleton of a cat. The angular position of the bones of the extremities necessitates muscular action to prevent collapse, as a result of the action of gravity.

to hold the knee and the hip extended to a degree which permits the trunk, thigh and leg to be in practically a straight line, that man is able to maintain the attitude and character of a human being. It is estimated that the gluteus maximus, the hip extensor, constitutes about 19 per cent of the musculature about the hip joint in man, while in the primates that can walk on their hind legs alone, as the gorilla, it constitutes about 15 per cent. But in addition, and even more important than its bulk, there is the power which man has acquired and apes have not, namely, that of using the gluteus to extend the hip joint so that the body and the thigh are approximately 180 degrees to each other. Similarly, in regard to the extensors of the knee, man has acquired the power of extension to a nearly straight line, a thing which even the primates cannot do.

It is natural, therefore, appreciating man's peculiar endowment in regard to the movement of the hip and knee, that in the correction of improper body mechanics, the full extension of these two joints should be of prime importance, and that from these joints as a point of departure work should begin.

A consideration of the skeletons of the pronograde animals and of the primates, which stand with bent knee and hip, immediately gives one

Fig. 3.—Skeleton of a man. Vertical flexibility is practically absent save in the feet.

the impression that their standing must be active, due to muscles, that is, or else they would collapse. Because man has trunk, thigh and leg in approximately the same line and has retained only in his feet a flexibility which permits of up and down movement, it should not be taken for granted that his weight rests on his lower extremity as on a column and that his feet bear weight by virtue of a combination of arches. It is much more logical to think that he, too, animal like the rest, stands by the activity of muscles, and uses the large muscles of the hip and thigh

in a mechanism, modified, but not essentially different from that of his lower animal associates.

I have long felt that a correct conception of the use of the lower extremity in standing must be one which regards this lower extremity as actively pushing the trunk away from the ground, and which looks on the foot not as the pedestal of a supporting shaft, but as the end member of an active positional and locomotor organ.

Observations of the behavior of children who were being trained in making the proper voluntary associations of muscles have brought this out clearly, and have given indication of the existence of a latent complex mechanism, which, given an opportunity, will of itself direct the associations and produce the desired body position.

It was noted first that some children early in their reeducation, without knowing what was desired of them, would bring into play, with the

Fig. 4.—Boy lying prone, kicking his lower extremity upward. This child was photographed at his first visit. He had had no training whatever and naturally no appreciation of the mechanics of the body. The position of the lower extremity, which shows extension at the knee, plantar flexion and inversion of the foot is therefore unconscious as to the muscular associations employed.

group of muscles being worked on, other muscles, which it was my intention, for reasons of mechanical advantage, to bring into association later. Unconsciously, they anticipated my instruction. The body seemed to know what I wanted it to do and to be trying to do it. I could not help but feel that however correct my ideas might be as to what should be done, the bodies of these children knew it all before me.

For instance, an untrained child, who could not contract the hip extensor, could, when lying on his abdomen, kick the lower extremity upward (extension). When he did this, he contracted the gluteus, extended the knee, plantar flexed the foot and inverted it strongly. At the same time the ribs on the opposite side were seen to separate and the muscles around the opposite shoulder girdle could be seen to con-

tract; this contraction would be stronger in proportion as the kick was made against resistance.[2]

A similarly untrained child, if he happened to be able to contract the glutei, or as I call it "pinch," would, when he made this effort, again, but on both sides, extend the knee, plantar flex the foot and invert it. In addition an outward rotation and adduction of the thighs was observed, and above the pelvis there was extension of the lower lumbar spine, retraction of the lower part of the abdomen, extension of the dorsal spine and widening of the intercostal spaces (thoracic cage elevation), with usually an evident contraction of the muscles around the shoulder girdle.

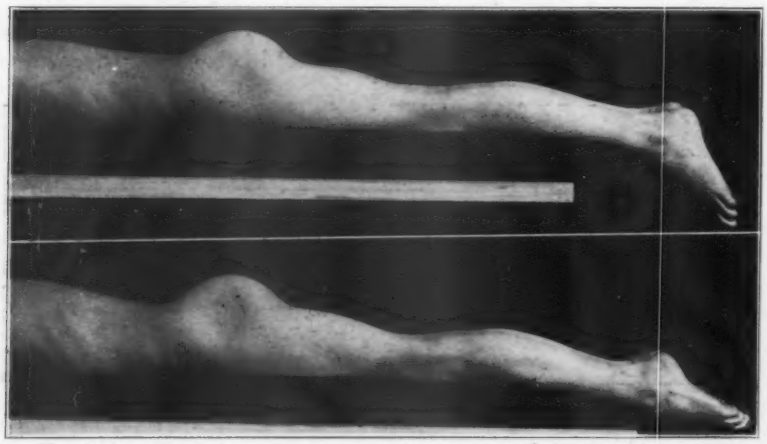

Fig. 5.—The same child as in figure 4, at the same visit. In the upper view, he is lying quite relaxed. In the lower view, he has responded to the request to "pinch" or make himself "hard" where two fingers have touched his buttocks. Note the evidence of gluteal contraction in the dimpling and the change in the curve of the buttock. The change due to extension of the knee is not apparent because in both views the knee is kept extended by gravity; the thigh, however, is thicker. Note change in position of the feet, the deepening of the thorax and the widening of the intercostal spaces. The retraction of the lower part of the abdomen and the extension of the lower lumbar spine is not brought out in this picture perhaps because the contraction is not very strong. It was evident in later pictures.

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2. The muscles about the shoulder which contract in response to this extensor effort of the opposite lower extremity are those which in the pronograde animal holds up the trunk as in a sling between the fore legs, which extend the foreleg on the shoulder and which keep the elbow stiff. They are the levator scapulae, the rhomboids, the serratus, the latissimus, the infraspinatus, one or both teres, the posterior part of the deltoid and the triceps. In the child lying on his abdomen, the triceps contracts usually only if the kick is resisted.

When a child has learned to make a bilateral gluteal contraction in the erect position,[3] the thighs become adducted, the knees extend and turn outward, the weight is borne on the outer side of the foot and on the outer four toes, leaving the great toe hardly touching the ground, and the feet are held in the inverted or "strong" position. Weak feet are corrected and apparent bow-legs are made straight. There may or may not be changes, at first, above the pelvis.

This movement reproduces, in the erect position, the unconscious associations of the muscles mentioned. It throws the body, as far as the pelvis and lower extremities are concerned, into the optimum posi-

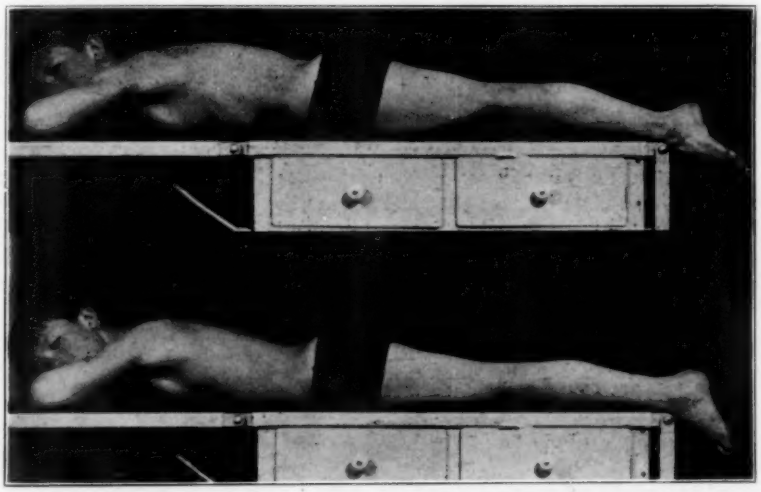

Fig. 6.—This boy has been trained and his associations are active; but he is consciously repeating only the "pinching" done by the untrained boy of figure 5. If turned so that he seems standing, these pictures show besides what is apparent in figure 5, the extensor effort at the knee, the retraction of the lower part of the abdomen, the elevation and widening of the thorax even against gravity and the flattening of the lumbar curve.

3. The ability of children to initiate contraction in the groups of muscles desired is usually excellent in the reptilian or in the pronograde positions or even with the head in its normal relationship to space as in the sitting position, which is that of the kangaroo, where the organs of equilibrium and the distance receptors of vision and hearing occupy their normal human position, but where the lower extremity still retains a position of flexion on the trunk and is not called on for weight bearing. With the assumption of anything like the extended position of the thigh, and the bearing of weight, the ability becomes much less great and is often nil. Children often manifest a complete inability when erect to do what they have done with complete facility a moment before in the positions of lower animals.

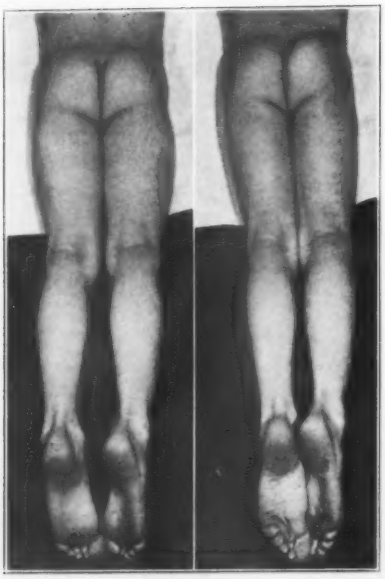

Fig. 7.—Same child as in figures 4 and 5 taken from above while relaxed and while pinching. Note in the right hand picture the contraction of the glutei, the activity about the knee, the adduction and outward rotation of the thighs and the plantar flexion and inversion of the feet, the latter a little more marked in the right foot. There is evidence of straightening of the line of the whole lower extremity with disappearance of the false look of knock-knee and bow-leg.

Fig. 8.—Same untrained child; end view while "pinching." Note the effect of the mechanism initiated by voluntary gluteal contraction on the position of the foot—plantar flexion, inversion, accentuation of both longitudinal and transverse arches and "gripping" effect of outer four toes. There is a "cerebral" quality about these feet which makes them suggest hands placed ready to catch a ball.

tion from the mechanical point of view and must be regarded, I think, as the active standing mechanism for man. Incidentally, it indicates the proper way to cure the flexible weak feet of children.

Another observation was that a child on all fours—the "cat" position —in which he flexes the pelvis to about 45 degrees from the line of the thighs and then forcibly extends it to 145 or 150 degrees, in extending the pelvis will unconsciously retract the lower part of the abdomen and widen the intercostal spaces. In making this movement, he is taught to keep the shoulder girdle high and rounded because it has been found

Fig. 9.—The "standing mechanism." The picture at the left shows the position of relaxation. This child is standing with glutei relaxed and pelvis tilted forward. Note the position of the knees in internal rotation; the apparent bowing of the legs due to the presentation in front of the posterolateral curve of the calf as a result of this inward rotation; the sharp curve below the inner aspect of the knee giving a false appearance of knock-knee, and the pronated feet.

The picture at the right shows the same girl a moment later when she had contracted the glutei and thrown the mechanism into action. Note the general straightening of the lower extremity with disappearance of bow-legs and knock-knee and the perfect position of the left foot. The right foot was not held straight ahead and as a consequence the righting effect from above was not exerted on this foot to throw the weight on to the outer toes and bring about inversion. (Reason for the teaching of straight foot walking.) Note also adduction of the thighs, activity of knee extensors and rotation outward of patellae. This action reproduces with the modification due to weight bearing the movements and muscle associations of figures 4, 5, 7 and 8.

that if he does so, the extension of the pelvis is to a higher angle. He may keep the upper extremity stiff at the elbow, but he is likely, unless reminded, to bend the elbows and relax the shoulder girdle. The natural tendency is to raise the head when the back is dropped and to bend it downward as the back and pelvis are raised to the position of "the cat on the fence." With this raising comes a supporting effort of both upper extremities and shoulders.

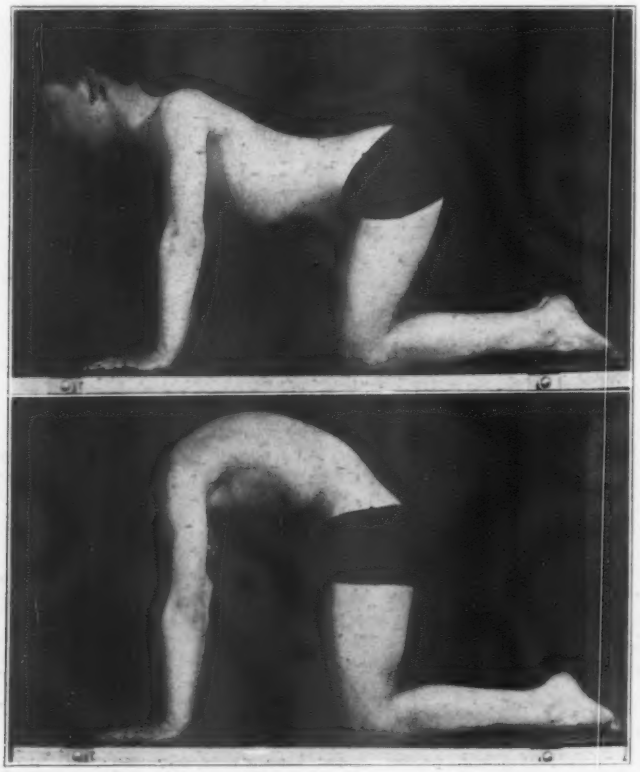

Fig. 10.—Retraction of the lower part of the abdomen when the back is high. The widening of the thorax which is also evident is better seen when the child is viewed from above. The supporting effort of the arm and shoulder girdle is also seen. Note the position of the head in the two positions. This child is trained but is reproducing what may be seen in the untrained child.

In the sitting position, when from a flexion of about 45 degrees to the thigh the pelvis is rocked backward to 90 degrees—45 degrees of extension—a child will unconsciously extend the dorsal spine, elevate and widen the thoracic cage and retract the lower part of the abdomen.

A child in a standing position, who is made to drop his head back as far as possible so as to extend the lower cervical spine, and then is made to, or helped to lift his head to a level position without carrying

the ears forward, a manoeuver which straightens by flexion but does not over flex the upper cervical vertebrae, will at the same time unconsciously move the knees out and invert the feet, as well as elevate and widen the thoracic cage. Extensor effort may be felt, also in the gluteus and the quadriceps extensor.

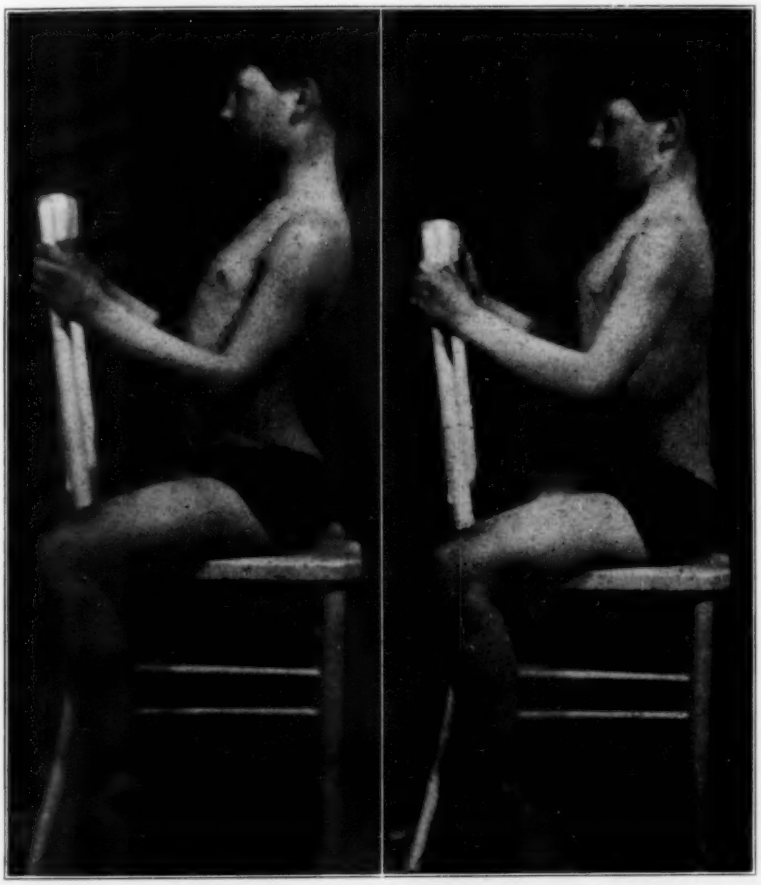

Fig. 11.—Trained child reproducing movement of untrained child. With the rotation backward of the pelvis, the lower part of the abdomen is retracted, the thorax widened, deepened and elevated and the dorsal spine extended. The good position of the head in this picture is seldom seen unconsciously produced.

These and other unconscious movements, which reproduced without training what I had been accomplishing in other children by training, made it almost certain that an underlying mechanism was at work, and I turned for confirmation of this idea to neurologic and physiologic literature, with which I had been unfamiliar.

In the vast literature on the physiology of muscular activity, there is a great deal which deals with the physiology of body position and the posture of animals. Beginning with his article of 1898, on decerebrate rigidity and reflex coordination of movements, Sherrington and his followers have made many contributions toward the explanation of of how animals stand and maintain their position in relation to space and how they adapt themselves to changes in their environment.

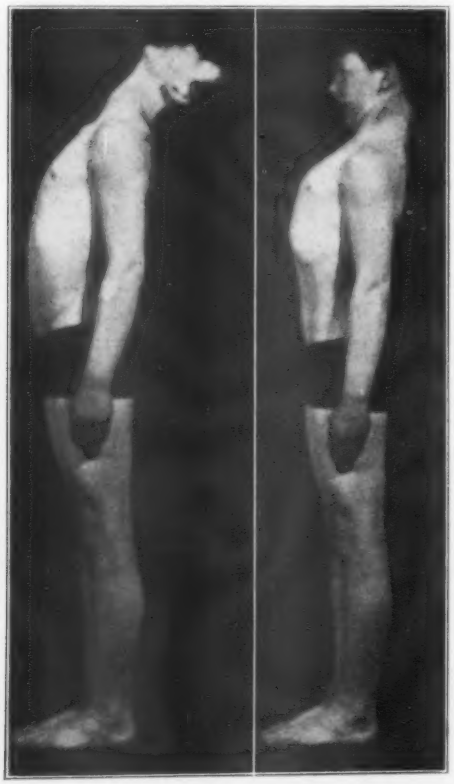

Fig. 12.—Trained child in position to elicit tonic neck reflexes by extending lower cervical spine, then flexing upper cervical spine and leveling head. An untrained child doing this will sometimes lose his balance because of the unwonted position brought about by the induced gluteal contraction and inversion of the feet. The position at the right is stiff from effort.

Among these investigators, perhaps no one has studied the subject more exhaustively than the late Rudolph Magnus of the University of Utrecht.

Magnus says in his Cameron Prize lecture:

The study of the physiology of movement is of old origin. Movement affords many points of attack for research because by movement changes in the condition

of the body or its parts occur which attract the attention of the observer and can be recorded or measured. This is not the case when posture is studied. Here we have to deal with a constant condition without apparent change so that our desire for causality is not stimulated and we therefore do not immediately suppose that active processes are at work. In consequence of this, the physiology of posture is of relatively recent date and many facts . . . have been discovered by still living physiologists during the last forty years, among whom Sherrington must be named in the first place. The chief results of these investigations is that posture is an active process and is the result of the co-operation of a great number of reflexes, many of which have a tonic character. Many parts of the central nervous system contribute to the function of posture; the importance of the spinal cord and the brain stem we understand up to a certain limit, whereas the activity of other parts, especially of the cerebellum and basal ganglia are still obscure.

An animal, the cat for instance, in which the cerebral hemispheres have been removed, enters into a state of increased muscular tone known as decerebrate rigidity, a condition which may obtain for some time. The attitude of the animal is that of extension of all four extremities and elevation of the head and tail. The tonic spasm is reflex, the stimuli coming from the muscles themselves and it is found in the anti-gravity muscles, their opponents having little or no tone. Thus, the spasm is confined to the muscles which keep the animal erect, and if it is placed on its feet it will stand, thus, as Sherrington says, disclosing an unmistakable biologic purpose for the reflex tone. Decerebrate rigidity is reflex standing. As far as the distribution of muscles goes, in the lower extremity it is the extensors of the hip and of the knee and the plantar flexors of the feet. In the decerebrate attitude as observed in the human being, the whole lower extremity is extended, the thighs adducted and the foot pointed down and inverted.

The identity of this attitude in animal and in man with the unconscious movement of the lower extremity already described and particularly with the "standing mechanism" is brought to your attention.

If a decerebrate animal has an irritant applied to its left hind foot, from which it would be natural for the animal in the intact state to wish to remove itself, the left hind limb will be flexed away from the source of irritation. The right hind limb will undergo an increase in extensor tone as if to undertake an added burden of support of the hind quarters; the left fore limb will also be thrown into greater extension, while the right fore limb will be flexed as if ready to take a step forward and away from the irritant. This is the crossed extension reflex, providing for the maintenance of the balance of the body under change in support, and for the coupling of the fore and the hind limbs of opposite sides as in normal locomotion.

In the contraction of the muscles of the shoulder girdle, when an extensor effort is made such as is seen in the child who kicks one leg upward, the other being relaxed (fig. 4), I think that a resemblance can

be seen to the extensor part of the crossed extension reflex. When bilateral extensor effort brings out simultaneous shoulder girdle contraction as in "pinching" or "the cat on the fence" the double reflex coupling of opposite sides is seen (fig. 5).

The experimental animal standing reflexly, if its head is forcibly depressed, will flex its fore limbs and increase the extension of its hind limbs. Its position is that of looking under a shelf. If the head is bent dorsally, there will be extension of the fore limbs and accompanying flexion of the hind limbs and sinking of the haunches as if it were looking up or were ready to leap for something in the air.

These last two movements illustrate two of the attitudinal neck reflexes which influence body position, ventroflexion stimulating extension of the lower extremity, while dorsiflexion diminishes it. These neck reflexes are in the three upper cervical vertebrae and are distinct from a reflex—the vertebra prominens reflex—which arises from the lower part of the cervical spine. Depression ventrally of this area results in flexion of all four limbs and head. It is evident in the action of an animal crawling into a hole. A dog sinks his head down between his shoulders, depressing this area, and with nose and belly on the ground, slinks into his kennel.

Attention is called to the child on all fours (fig. 10). If he lets the shoulder girdle drop, the extension of the pelvis is less effective, a possible effect of the vertebra prominens reflex. When he flexes the pelvis in dropping his back, he is likely to dorsiflex the head; when he extends the pelvis in raising his back, he bends his head forward and downward. These two natural movements correspond to the associations evident on forcibly moving the head to elicit the neck reflexes. Finally, the common observation that a child, unless warned, in endeavoring to perform the maneuver illustrated in figure 10, will bend the elbows and relax the shoulders, illustrates in the human being the position of the cat looking under a shelf.

The child, when he drops his head back and then raises it as in figure 12, unconsciously brings the extensor effort of the "standing mechanism" into play, and demonstrates the tonic neck reflex of ventroflexion affecting the extensor tone of the hind limb.

This last is undoubtedly also influenced by tonic reflexes which come from the labyrinths and which have been studied exhaustively by de Kleijn, collaborating with Magnus. These labyrinthine tonic reflexes are a function of the epithelium of the utricular maculae and are excited by the position of the otolithic membranes in relation to the epithelium. When the head of the animal is in such a position that the otolithic membranes exert a pull on the epithelium of the utricular maculae, these tonic reflexes cause a maximum of extensor effort in all four extremities and neck. At 180 degrees to this position, when the

otolithic membrane presses on the epithelium, the extensor effort is at a minimum. Between the maximum and the minimum position of the head, all grades of reflex tone may be obtained.

Labyrinthine tonic reflexes affect the whole body, including the neck. The reflexes of the neck affect all four limbs. So, on the hind limbs, for instance, there are two sets of influences which may operate with each other or against each other and in varying degrees, so that all degrees of antigravity effort may result.

In man, the normal position of the head in standing is about midway between the maximum and the minimum position for the labyrinthine reflexes. Their effect is hard to demonstrate in the human being, and I have not observed as yet any unconscious movements which I could with assurance relate to labyrinthine reflex control.

The similarity between the observations of the unconscious movements of children here recorded and the postural reflexes observed in animals by the physiologists, particularly the identity between the muscles employed in the "standing mechanism" and the reflex standing of the decerebrate animal, is sufficiently great, I think, to permit of the conclusion that in work for the correction of improper body position, the arrangement by which this should be accomplished was already planned out and existent in the central nervous system before the forebrain began the development which has made thinking man.

To use for the benefit of children's bodies this ancient and complex mechanism, harmony must be created between the manner in which the cortex directs the body and that which the lower centers have been accustomed to follow from time immemorial, so that the phasic control of the muscles may agree with the reflex control; so that the orders of the captain of the steamship—to borrow Beevor's simile—may enlighten and not confuse the engineer down below who alone can carry them out.

ACTIVATED ERGOSTEROL IN THE TREATMENT OF RICKETS *

SAMUEL KARELITZ, M.D.
NEW YORK

In an attempt to repeat the experiments of Hume and Smith,[1] Chick and Tazelaar [2] showed that it was not the irradiated air which cured the rachitic rats, but that the cure was effected through the ingested irradiated, excreta-soiled sawdust of the cages. Nelson and Steenbock [3] showed that nonirradiated rachitic rats kept in the same cages with irradiated rachitic rats were cured, not by the secondary rays emitted from the latter, but by the excreta which they ate. Steenbock and Black [4] induced antirachitic properties into rat rations by exposing the foods to ultraviolet rays. Hess [5] and Steenbock and Nelson [6] almost simultaneously reported the curing of rickets in rats by feeding irradiated food substances. Hess was successful in using irradiated rat skins as treatment for rickets. With irradiated liquid milk, Kramer [7] successfully treated infants who had rickets. Rosenheim [8] and György, Yenke and Popoviciu [9] confirmed the work of Hess and Steenbock and their co-workers.

Zucker [10] showed that only the nonsaponifiable fraction of cod liver oil was active; likewise, Koch, Cahan and Gustavson [11] showed that the nonsaponifiable fraction of cod liver oil was antirachitic. Hess [12] and Steenbock [13] independently found that only the nonsaponifiable fraction

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* Received for publication, July 19, 1928.

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13. Steenbock, H., and Daniels, A. L.: Irradiated Foods and Irradiated Organic Compounds, J. A. M. A. **84**:1093 (April 11) 1925.

of foods (consisting mainly of cholesterol in animal cells and phytosterol in plant cells) could be activated by irradiation. Hess and Weinstock,[14] Steenbock and Daniels,[13] and later Drummond, Rosenheim and Coward [15] cured rachitic rats with irradiated cholesterol, and György successfully treated rachitic infants with irradiated cholesterol. Hess also fed irradiated brain, because of its high cholesterol content, to rachitic rats, with curative effect.

Hess [14] reported that the transmissibility of irradiated cholesterol is greater for certain rays than that of nonirradiated cholesterol, and with prolonged irradiation this peculiar property disappears, as does also the antirachitic potency. Schlutz and Morse [16] found that oxidizing cod liver oil has a definite absorption spectrum between 280 and 300 milli-

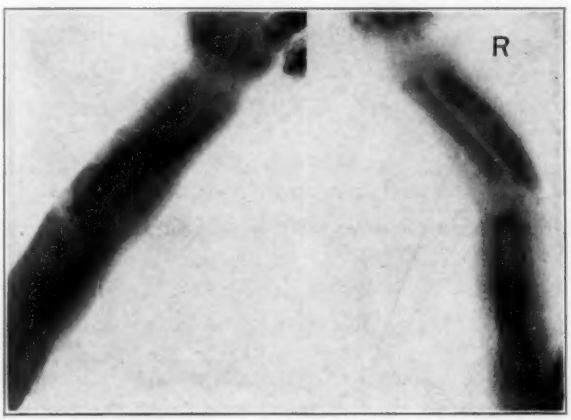

Fig. 1 (case D. R.).—Upper extremities, showing marked rarefaction of bone, extensive periosteal elevation and proliferation, especially of humeri and phalanges, moth eaten metaphyses, infractions of ulnae at lower end, enlarged cartilaginous epiphyses and indistinct centers of ossification of carpal bones.

microns, and Hess found the same to be true for irradiated cholesterol. It was then shown that the absorption spectrum of purified cholesterol is different from that of nonpurified cholesterol, and that the former cannot be made antirachitic by irradiation.

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14. Hess, A. F., and Weinstock, M.: J. Biol. Chem. **64**:181, 1925. Hess, A. F.; Weinstock, M., and Helman, F. D.: J. Biol. Chem. **63**:305, 1925; Proc. Soc. Exper. & Med. **22**:227, 319, 1924-1925.

15. Drummond, J. C.; Rosenheim, O., and Coward, K. H.: J. Soc. Chem. Ind. **44**:194 (March) 1925. Hess, A. F.: Antirachitic Activity of Irradiated Cholesterol, Ergosterol and Allied Substances, J. A. M. A. **89**:337 (July 30) 1927.

16. Schlutz, F. W., and Morse, M.: Spectroscopic Observations on Cod Liver Oil, Am. J. Dis. Child. **30**:199 (Aug.) 1925.

From observations made by Rosenheim and Webster,[17] Windaus, Pohl and Hess,[18] it was suggested that the provitamin was concentrated in the less soluble and less volatile fraction of cholesterol, also that it was more photosensitive than cholesterol itself and chemically less stable. Pohl and Windaus observed that this fraction gave the same absorption spectrum as did the oxidizing cod liver oil and nonpurified cholesterol. One-thirtieth of 1 per cent (0.033 per cent) of this substance, when radiated and added to purified cholesterol restores to it its spectroscopic property as well as its antirachitic potency. This contaminator comprised about from 0.05 to 0.02 per cent of the original cholesterol. Pohl and Windaus suggested that any substance which could be considered

Fig. 2.—The lower extremities, showing observations similar to those in figure 1. The osteophytic layering should be noted.

antirachitic should show the typical absorption spectrum. This same suggestion had been made before by Schlutz and Morse, with the idea of eliminating much experimentation on the rat.

17. Rosenheim, O., and Webster, T. A.: Biochem. J. **21**:127, 1927; Lancet **1**:306 (Feb.) 1927.

18. Pohl, R.: Nachr. v. d. k. Gesellsch. d. Wissenschr. zu. Götting. Math. Physik Klasse 1926, p. 85; Naturwissenschaften 1927, vol. 20. Windaus, A., and Hess, A. F.: Gesellsch. d. Wissenschr. zu Götting,, Jan. 28, 1927. Windaus, A.: Medicinische Gesellsch. Götting., Jan. 27, 1927; München. med. Wchnschr. **74**:345, 1927; Klin. Wchnschr. **6**: (March 19) 1927. Hess, A. F. et al.: J. Biol. Chem. **70**:123, 1926.

On testing a large series of known sterols, Windaus, Pohl, Hess, and Rosenheim and Webster found that the properties of activated ergosterol, formerly isolated from mushrooms, ergot and yeast, most closely fulfiled the requirements. Windaus named this substance provitamin D.

Rosenheim and Webster showed that as little as 0.001 mg. daily given to a rachitic rat cured the disease in about from ten days to two months. More recently, Hottinger and Rosenheim prevented rickets in rats by the administration of daily doses of 0.00001 mg. of activated ergosterol. Numerous experimenters, Hess and Windaus,[19] Holtz,[20] György,[21] Hottinger,[22] Lasch and Behrens,[23] Beumer and Falkenheim,[24] Strate,[25]

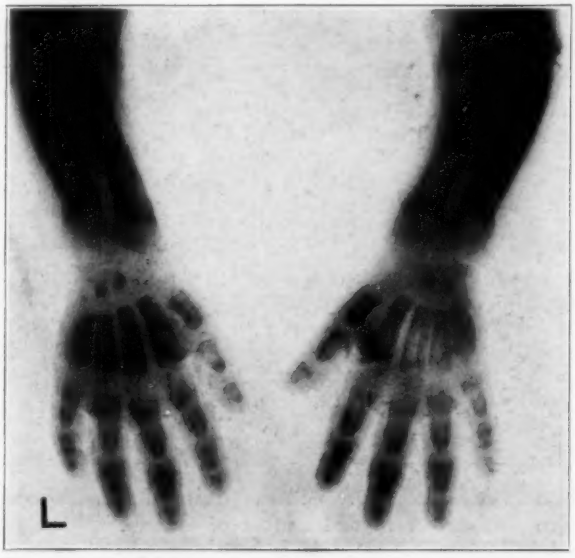

Fig. 3. (case D. R.)—After three weeks on 5 minims vigantol daily, showing increase of lime and deposit of the epiphyseal line.

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19. Hess, A. F., and Windaus, A.: Proc. Soc. Exper. Biol. & Med. **24**:171, 1926-1927; **24**:369, 416 (Feb.) 1927.

20. Holtz, F.: Das antirachitische Vitamin, Klin. Wchnschr. **6**:535 (March 19) 1927.

21. György, P.: Therapeutische Versuche mit bestrahlten Ergosterin, Klin. Wchnschr. **6**:580 (March) 1927; **4**:1118 (June 4) 1925; **5**:747 (April 23) 1926.

22. Hottinger, A.: Schweiz. med. Wchnschr. **56**:170, 1926; Klin. Wchnschr. **5**:2061, 1926; Ztschr. Kinderh. **43**:8, 1927; **44**:282, 1927.

23. Larsch, W., and Behrens, A.: Ueber die Wirkung des Ergosterins auf die Rachitis, Deutsche med. Wchnschr. **52**:1552, 1927.

24. Beumer, H., and Falkenheim, C.: Klin. Wchnschr. **6**:798 (April 23) 1927.

25. Strate, Hans: Klin. Wchnschr. **7**: (Jan. 15) 1928.

Sachs,[26] Beck,[27] Völckers and Blum,[28] Starlinger,[29] Vollmer,[30] Falkenheim,[31] Hess,[32] Aidin,[33] Vogt [34] and Shohl [35] reported their experiences, almost all of which were successful not only for rickets in rats, dogs and infants, but also for tetany in infants and in adults, rickets tarda and osteomalacia and prophylactically in rats on a rachitic diet and in premature infants. The reports of Starlinger, György and Hottinger include the results on patients with osteomalacia; the report of Vogt is especially devoted to prophylaxis.

Hess [32] has also had good results with irradiated brain and yeast, the latter in dosages of from 0.5 to 1 Gm. of the dried, irradiated

Fig. 4 (case D. R.).—After five weeks of treatment, showing general increase of lime, tendency to resume normal contour of bones, sharp epiphyseal lines of phalanges and filling in of metaphyses and widening of epidiaphyseal line.

26. Sachs, F.: Neueres uber die Rachitis, Hessischen Aertsteblatt, 1927, no. 13.

27. Beck, W.: Für die Behandlung der Rachitis mit bestrahlten Ergosterin, Die Therapie der Gegenwart, 1927, vol. 9.

28. Volckers, H., and Blum: Beobachtung uber die Heilwirkung bestrahlten Ergosterin bei V, Med. Klin., 1927, no. 37.

29. Starlinger, W.: Ueber die Beeinflussung des Verlaufes einer schweren Osteomalazie durch bestrahltes Ergosterin, Deutsche med. Wchnschr. **53**:1553, 1927.

30. Vollmer, H.: Beitrag zur Ergosterin Behandlung der Rachitis, Deutsche med. Wchnschr. **53**:1634 (Sept. 23) 1927.

31. Falkenheim, C.: Zur Therapie der Säuglingsrachitis mit aktiven Ergosterinpräparaten (Vigantol), Deutsche med. Wchnschr. **53**:550, 1927.

32. Hess, A. F.: Antirachitic Activity of Irradiated Cholesterol Ergosterol and Allied Substances, J. A. M. A. **89**:337 (July 30) 1927.

33. Aidin, R.: Lancet **1**:229 (Feb. 4) 1928.

34. Vogt: München. med. Wchnschr. **75**:721 (April 27) 1928.

35. Shohl, A. T.: Proc. Soc. Exper. Biol. & Med. **25**:576, 1928.

substance daily for infants and of from 10 to 25 mg. for rats. Kramer [36] likewise obtained good results with dried, irradiated yeast in rachitic rats. Vollmer [37] recently showed that single large doses of activated ergosterol cured animals that had rickets, thus proving that the animals could store this vitamin.

Activated ergosterol has antirachitic power 20,000 times as great as that of cod liver oil, that is, 1 mg. is the equivalent of 20 Gm. of cod liver oil. It can be activated in a medium of nitrogen, absolute alcohol, petroleum ether, liquid petrolatum, and in vacuum when radiated for one-half hour with a magnesium spark or quartz mercury vapor lamp. Its greatest activity comes after twelve hours of irradiation. Further radiation decreases its activity so that after eighty hours of exposure to ultraviolet rays it is no longer antirachitic. It does not

Fig. 5.—Observations corresponding to those in figure 4 except for the prominence of the old centers of tarsal bones as in healed scurvy.

retain its antirachitic power if exposed to air for a long time because of oxidation. It shows a specific absorption spectrum between 280 and 300 microns; this observation caused it to be recognized as the antirachitic substance or provitamin, so named by Windaus.

Activated ergosterol in oil as vigantol (prepared by I. G. Farben Industrie, Leverkusen, Germany) and later the first American product of the Winthrop Chemical Company was used. My report deals with the results obtained in eleven cases of rickets (patients previously untreated) of all degrees both in white and in colored children, in one case of tetany and in one case of marked osteoporosis and atrophy

36. Kramer, B., and Shear, M. J.: Proc. Soc. Exper. Biol. & Med. **25**:285 (Jan.) 1928.

37. Vollmer, H.: Ztschr. f. Kinderh. **45**:265 (Feb.) 1928.

of the bone caused by disuse and with the results obtained when the drug was used for erophylaxis in three new-born infants. The diet of these children was almost exclusively milk, sugar, water and cereal—with the exception of that for the older children who were given mixed diets.

RESULTS

The results, as shown in the accompanying table, are based on clinical, roentgenologic and, as far as was possible, on chemical data, and show almost invariable success—that is, all but one child showed evidence of healing rickets within three weeks of daily treatment with activated ergosterol. Treatment was conducted between November, 1927, and February, 1928. The blood calcium and phosphorus were

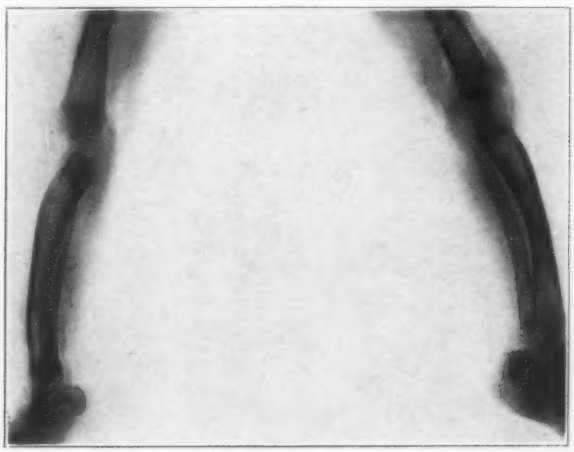

Fig. 6.—Picture taken four months after cessation of treatment, or four months later than that in figures 4 and 5. It shows general increase in lime, tremendous growth in length, marked calcification of epidiaphyseal lines and tendency to correction of shape of shaft with heavy cortex. Note distance from epiphyses to diaphyses as compared to earlier roentgenograms as well as increase in visible carpal centers.

determined by the Kuttner colorimetric method. A few calcium determinations were checked by the Kramer-Tisdal method.

In giving the results, I refer to the x-ray evidence of rickets as general poverty in lime, irregular and cupped metaphyseal line, large cartilaginous zone between epiphyseal center and diaphyses and periosteal proliferation, the latter being mentioned especially when present.

By x-ray evidence of healing I refer to general increase in lime, a deposit of a white line of calcification at the metaphysis furthest away from the diaphysis—gradual filling in of this space with lime, correction of shape of the epiphyses of lime deposit and filling in of the periosteal proliferating zone.

X-Ray Observations in Fifteen Subjects

Name	Age	Illness	Evidence of Rickets: Craniotabes	Ribs	Wrists	Bowlegs	X-Ray	Daily Vigantol in Minims	Admission: Calcium	Admission: Phosphorus	Later: Calcium	Later: Phosphorus	Results
1. H. M.	5 mo.	Anemia	++	+	++	+	++	5	10	3.4	8.2 in 14 days	4	Craniotabes healed in 12 days; wrists healing by x-ray in 21 days
2. E. N.	7 mo.	Pneumonia	+++	++	+++	++	+++	5	9.5	2.0	9.8 in 14 days	4.2	Craniotabes healed in 14 days; early healing of long bones in 18 days, complete in 6 weeks
3. J. G.	7 mo.	Pneumonia	++++	++	+++	++	+++	10	8.8	3.2	9.6 in 14 days	5.5	Craniotabes healed in 7 days; x-ray evidence of healing of wrists in 21 days
4. E. C.	6 mo.	Upper respiratory tract	++++	+++	+++	.....	+++	5	9.6	4.0	8.9 in 30 days	4.9	Craniotabes healed in 14 days; x-ray evidence of healing in 21 days
5. W. R.	7 mo.	Pneumonia	++	++	++	+	++	5	7.9	3.0	8.2	3.6	Craniotabes healed in 21 days; x-ray evidence of healing in 21 days
6. D. R.	2 yr.	Pneumonia	Anterior fontanel 4 × 3 cm.	++++	++++	++++	++++	5	8.3	3.8	8.7 in 14 days 8.8 in 24 days 7.7 in 30 days	5.1 4.0 4.1	Fontanel became filled in; x-ray healing in 18 days, and progressively improving; incompletely healed in 8 weeks
7. C. B.	2 yr.	Rickets	.....	+++	++++	++++	+++	5	9.6	3.4	9.2 in 12 days	4.6	X-ray evidence of healing in 17 days
8. Baby A.	3½ mo.	Rickets	++++	.....	++	.....	.....	5	...	...	...	...	Craniotabes healed in 3 weeks
9. Baby O.	3 mo.	Rickets	++++	.....	++	.....	.....	7	...	...	...	...	No result in 2 weeks; thickening in 4 weeks; hardening in 6 wks.
10. D. R.	6 mo.	Rickets	++++	++	+++	+	+++	5	...	...	...	...	Craniotabes healed in 7 days; x-ray evidence of healing in 12 days
11. G. C.	5 mo.	Bronchopneumonia, tetany, rickets	+++	++	++	.....	+++	10	6.0	2.6	8.9 in 12 days 8.2 in 21 days	3.5 6.9	Craniotabes healed in 10 days; x-ray evidence of healing in 18 days; no further convulsions; Chvostok sign absent after 14 days
12.	.....	Periarteritis nodosa	.....	.....	.....	.....	Marked Atrophy and bone osteoporosis	15	10.0	4.1	9.6	4.4	No change in a month
13. 14. 15.	Three infants born in January receiving 5 minims vigantol, still fail to reveal any evidence of rickets												

Depending on the number of the aforementioned conditions and their degree, I refer to the condition as mild, moderate or severe. When the epidiaphyseal space is completely obliterated by lime, and when the cortex does not show further periosteal lifting off or proliferation, I call the condition healed.

I have designated the severity by + to + + + + or from mild to extremely severe rickets.

Case 3 is noteworthy because of the healing of craniotabes in seven days; case 9, because of the persistence of craniotabes even after the patient had been given 7 minims of vigantol or 5 mg. of activated

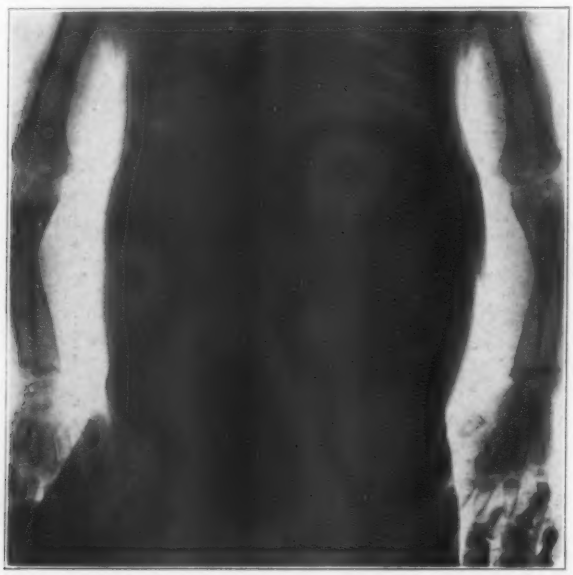

Fig. 7.—This picture shows the same features in the upper extremities as are seen in figure 6 for the lower extremities.

ergosterol daily for four weeks; and case 12, because of marked atrophy of the bone and osteoporosis without response to 1 cc. vigantol daily for one month.

The patient in case 6, a colored boy, aged 2 years, was moribund, with a widespread bilateral bronchopneumonia involving all lobes. The anterior fontanel was 4 by 3 cm., the head was large, the clavicles curved anteriorly and upward, and the chest showed marked deformity, being narrow and deep anteriorly with the sides caved in. A large rosary, a deep Harrison's groove, pot belly and a large, firm spleen and enlarged liver 4 cm. below the border of the rib were present. The upper and lower extremities were markedly curved, with irregular

masses palpable at the lower third or half of both humeri and the right ulna, probably due to callous formation.

The blood calcium and phosphorus two days before, and twelve, twenty-two and thirty-nine days after the beginning of treatment were as follows: calcium, 8.3, 8.7 8.8 and 7.7; phosphorus, 3.8, 5.1, 4 and 4.1.

X-ray examination revealed an extreme type of rickets, with diffuse lack of lime, indistinctness of the epiphyses and large spaces between the epiphyses and diaphyses, numerous nicks as if there had been infractions in the humeri and ulnae and marked periosteal proliferation with the cortex of the shafts of the long bones indistinct and occurring in strips. The marked and symmetrical periosteal changes, the phalangeal and metacarpal periosteal elevation and the general lack of lime resembled syphilitic periostitis and dactylitis so much that, despite

Fig. 8 (case E. N.).—Marked irregularity of metaphysis, cupping and large areas of cartilage and general poverty of lime.

the negative Wassermann reaction of the blood of the patient and all other members of the family, syphilis plus rickets was considered the most likely diagnosis until the results with antirachitic therapy alone were observed.

The patient received activated ergosterol for eight weeks. No untoward effects were observed during treatment or during the following four months. Six months after therapy was started, the x-ray pictures revealed marked increase in calcification, tremendous growth in length, and possibly excessive calcification at the epidiaphyseal lines and in the new cortex of the femora.

COMMENT

My results agree with those reported by others. All but one of the patients showed healing following the administration of a daily

dosage of 5 minims or 0.33 cc. of vigantol or 3.33 of activated ergosterol in oil, given over a period of from three to eight weeks. Thus a colored child, aged 7 months, who had craniotabes with moderately severe rickets was definitely improved in seven days following the administration of 6 mg. daily, and the condition healed in ten days. One author reported clinical improvement in a patient with craniotabes in six days, but most investigators found that it took from fourteen to twenty-eight days; however, the doses of activated ergosterol were smaller than those given to this child. The other children showed healed craniotabes in from fourteen to twenty-one days. X-ray evidence of healing in the long bones was seen as early as in twelve days, but it usually required three weeks. Others obtained results as early as

Fig. 9.—The same bones as shown in figure 8 after six weeks of therapy, showing increase of lime generally, a fine epidiaphyseal line and distinctness and increase in size of carpal centers of ossification.

in ten days, but in most cases they were not obtained until after from eighteen to twenty-one days. Patients with tetany were cured in fourteen days.

Healing took place despite complicating diseases, such as pneumonia or grip. The general disposition of the children seemed to improve after two weeks. In the mild and moderate cases of rickets, a complete filling in of the metaphyses occurred in about six weeks, but in an extreme case (D. R., case 10) the condition had not completely healed in eight weeks, although each week after the third a definite and marked improvement was seen over the preceding observations. The blood calcium and phosphorus usually returned to the normal amount within about two weeks. There did not seem to be any difference in the results obtained with the German and with the native preparations of vigantol.

Activated ergosterol is also being used in cases of fracture and to stimulate healing of wounds. It is also prepared in pill or chocolate tablet form. All of these products have been reported to be equally effective.

Recent work performed simultaneously in Hungary [38] and in this country [39] shows that purified cholesterol, even the original preparation of Windaus and Hess, when given in doses thirty times as large as the ordinary dose used, exhibits some activity. This raises the question whether all the activated ergosterol was removed in the process of purification, whether the cholesterol has a slight antirachitic value when radiated, or whether it might be some other sterol or contaminator of cholesterol besides ergosterol which can be activated as Hess suggested.

Kreitmair and Moll [40] have recently shown the dangerous effects of an overdose of activated ergosterol in rats, dogs, rabbits, guinea-pigs and chickens. The pathologic changes were mainly rich layers of calcium in the walls of the blood vessels, heart muscle, stomach, lungs, kidneys and spleen. When smaller doses of activated ergosterol were used, the toxic effects were not elicited. These authors point out the unlikelihood of any ill effect from the minute doses which are adequate for prophylaxis or cure of rickets, tetany or osteomalacia in man, since doses 200 times greater than that needed for clinical results were necessary before toxic symptoms were observed. Therapeutically, from 2 to 5 mg. irradiated ergosterol daily is usually adequate, and prophylactically from 1 to 3 mg. daily suffice. The dosage may be judged according to the age and size of the child, degree of rickets and complicating diseases. These suggestions are based on the experiences of various authors and not founded on personal observations.

Since healing continues after treatment has ceased and since, according to Vollmer, ergosterol is stored, I believe that the administration of activated ergosterol may be discontinued after a period of from three to six weeks regardless of the stage of healing present at the time. This may be a manner of avoiding toxic results of excess activated ergosterol. Whether or not healing will cease or recede in some cases can be answered only by experience.

Shittenhelm and Eisler [41] have now opened a new phase in the study of vitamin D which casts doubt on the idea that activated ergosterol is really provitamin D or that ultraviolet light is absolutely necessary to activate any substance potentially antirachitic. They showed that barley seeds which did not contain any ergosterol and which were not

38. Jendrassik, A., and Kemenyffi, A. G.: Zur Kenntnis des D-Vitasterins; II Ueber die Aktivierbarkeit des Cholesterins, Biochem. Ztschr. **189**:180, 1927.

39. Bills, C. E.; Honeywell, E. M., and MacNair, W. A.: J. Biol. Chem. **76**: 261 (Jan.) 1928.

40. Kreitmair and Moll: München. med. Wchnschr. **75**:637 (April 13) 1928.

41. Shittenhelm, A., and Eisler, B.: Klin. Wchnschr. **7**:1118 (June 10) 1928.

antirachitic became antirachitic during the process of germination, at which time ergosterol was not detectable. Voltz [42] has reported similar results with grass (*Lolium perenne*). Germination occurred in the dark, so that extrinsic ultraviolet light could not have been a factor. If this is true, a new explanation as to what vitamin D is will have to be offered.

A preliminary report of this study was published in the Proceedings of the Society for Experimental Biology and Medicine, April, 1928, volume 25, page 576.

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42. Voltz, cited by Shittenhelm, A., and Eisler, B.: Klin. Wchnschr. **7**:1118 (June) 1928.

VALUE OF LIVER EXTRACT (343) IN IDENTIFYING AND IN TREATING CERTAIN ANEMIAS OF INFANCY AND OF CHILDHOOD

REPORT OF A CASE OF PROBABLE PRIMARY ANEMIA IN AN INFANT NINE AND ONE-HALF MONTHS OLD *

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SAN FRANCISCO

Holt and Howland [1] in the last edition of their textbook, remarked: "The existence of primary anemia (pernicious anemia) in children is very doubtful. A number of cases have been reported but they do not, as a rule, bear critical analysis." In a review dated 1918, von Seht [2] concluded that the youngest authentic case is that of Kusunoki [3] whose patient was 6 years old at death. Although Kusunoki's patient presented a characteristic clinical picture of acute purpura hemorrhagica, the condition of the blood and the results of the postmortem examination appear to justify a diagnosis of pernicious anemia. Since von Seht's review, two other reports have been published concerning still younger children in whom the blood picture and necropsy observations were highly suggestive if not fully conclusive of primary anemia. One of these is reported by Vischer.[4] The patient was 3½ years of age at the onset of symptoms, and 4½ years old at the time of death. Careful studies of the blood were made during life, and a thorough necropsy, including histologic studies, is described. Fanconi [5] presented in even greater detail the case histories and necropsy observations of three brothers; in the first, the onset of symptoms occurred when he was 5½ years old; in the second, the onset occurred at the same age and death at 7, and in the third, the symptoms began when he was 4 years old and death occurred when he was a little less than 5 years. In all, the postmortem diagnosis was pernicious anemia.

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* From the Department of Pediatrics, Stanford University School of Medicine. Various members of the pediatric staff assisted in obtaining the data on which this paper is based.

1. Holt, L. E., and Howland, J.: The Diseases of Infancy and Childhood, ed. 9, New York, D. Appleton & Company, 1926, p. 694.

2. Von Seht, L.: Ueber kryptogenetische Biermersche Anämie im Kindesalter, Ztschr. f. Kinderh. **18**:15, 1918.

3. Kusunoki, M.: Die perniziöse Anämie im früheren Kindesalter, Cor.-Bl. f. schweiz. Aerzte. **44**:833, 1914.

4. Vischer, D.: Perniziöse Anämie in Frühen Kindesalter, Schweiz. med. Wchnschr. **4**:1104, 1923.

5. Fanconi, G.: Familiäre infantile pernizioaartige Anämie (perniziöses Blutbild und Konstitution), Jahrb. f. Kinderh. **117**:257, 1927.

There are not any authentic cases of primary anemia on record in which death occurred at an age of less than 4½ years. It is not established, however, that the disease does not occur at an earlier age. The fact is that a few patients under 1 year of age have been reported in whom the blood picture was highly suggestive. The real difficulty has been the lack of adequate corroborative data, such as are usually considered necessary for the establishment of a cumulative diagnosis, that is, a diagnosis which can be made only by the blood picture plus one or more other characteristic conditions. Thus, Cornell [6] stated that the one obligatory feature of a diagnosis is achlorhydria, which occurs in practically 100 per cent of the cases of pernicious anemia, not infrequently antedating the changes in the blood. One or more other characteristic features should also be on record, such as nervous involvement, glossitis, gastro-intestinal symptoms, urobilinogen in the urine, increased urobilin output, decreased fragility of the red blood cells, delayed direct van den Bergh reaction and increased volume index. In young children and infants, collection of the gastric secretion is technically difficult and is seldom made; nervous symptoms rarely are analyzed in much detail, and tests requiring more than 1 or 2 cc. of blood (until recently) have not been attempted.

In cases occurring in infancy and in early childhood reported in the past it has been necessary to rely on the observations made during ordinary examinations of the blood and postmortem study. Critics have been forced to reject, as unproved, all cases in which necropsy was not performed. Nevertheless, the examinations of the blood in the cases reported by Naegeli [7] (5½ months old infant), von Starck [8] (6 months old infant), Koch [9] (8 months old infant) and Sochorowitch [10] (9 months old infant)—to mention only those of patients under 1 year of age—revealed pictures closely resembling that of true primary anemia.

Granted the similarity, it may be suspected either that the disease may have been a true primary anemia, or that it had as a common feature with the latter the defective erythroblastic maturation in the

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6. Cornell, B. S.: Pernicious Anemia, Duke University Press, 1927.

7. Naegeli, O.: Blutkrankheiten und Blutdiagnostik, ed. 4, Berlin, J. Springer, 1923; cited by Vischer (footnote 4).

8. Von Starck, W.: Die basophile Granulation (Punktierung) der roten Blutkörperchen im embryonalen Blut und bei anämischen Zuständen im Kindesalter, Jahrb. f. Kinderh. **69**:264, 1909.

9. Koch, G.: Ueber perniziöse Anämie und extramedulläre Blutbildungen im Säuglingsalter, Jahrb. f. Kinderh. **71**:140, 1910.

10. Sochorowitch: Ueber einen Fall von tödlicher Kinderanämie (Perniziöse Anämie?) mit erythropoese und myeloider Umwandlung der Milz und Lymphdrüsen, Inaug.-Diss., Zürich; cited by Vischer (footnote 4).

bone marrow which Peabody [11] has recently described as occurring so constantly in pernicious anemia. The latter hypothesis at least can now be put to direct test. The administration of liver and particularly the fraction of liver isolated by Cohn, Minot and their collaborators,[12] specifically promotes the maturation of the megaloblasts, and this is shown, as Minot and Murphy [13] pointed out, by a characteristic transient rise in the circulating reticulocytes and an increase in the red blood cells.

In the last seven months at Lane Hospital, there has been an opportunity to make the test with liver extract in three cases of severe anemia with high color index and some other features suggestive of primary anemia. Two of the patients were less than 1 year old and the third was a little less than 5 years.

REPORT OF CASES

CASE 1.—*History.*—C. D., a girl, born on Jan. 14, 1927, was admitted to the hospital on Oct. 4, 1927, on account of pallor, constipation, vomiting and loss of weight. The father and mother were living, 26 and 20 years old, respectively. The father was well; the mother was said to have heart and kidney trouble. The patient was the first child, and there had not been any other pregnancies. The infant had been born at full term, following thirty-six hours of labor; delivery had been instrumental, and the infant had weighed 6¾ pounds (3 Kg.).

The infant had been breast fed for two months, and since then had been fed goat's milk and water with various sugar additives. Orange juice was begun at 2 months of age and cereals at 9 months. Vegetables and other foods had not been given. The baby had held up her head at 3 months, and had sat alone and cut her first tooth at 6 months. The cleanliness and general care of the baby were open to suspicion. Save for one attack of diarrhea, the child had always been constipated. On the whole, she had been well up to the age of 6 months, at which time she had weighed 12 pounds (5.4 Kg.). A month before admission she had weighed 16 pounds (7.3 Kg.).

At 6 months of age, while cutting the first tooth, the child had begun to have from six to eight loose stools daily. This persisted, with periods of improvement, for about two weeks. Afterward, she had been constipated, passed a good deal of gas from the stomach and bowels, and was seen to be markedly distended. Regurgitation of from one half to two thirds of the bottle had become increasingly frequent, but projectile vomiting had not occurred. The baby had always been pale, but during the last three months, the pallor had become increasingly marked, and increasing weakness had occurred during this period. The mother thought that the infant had lost 2 or 3 pounds (0.9 or 1.4 Kg.) during the month before admission.

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11. Peabody, F. W.: Pathology of Bone Marrow in Pernicious Anemia, Am. J. Path. **3**:179, 1927.

12. Cohn, E. J.; Minot, G. R.; Fulton, J. F.; Ulrichs, H. F.; Sargent, F. C.; Weare, J. H., and Murphy, W. P.: The Nature of the Material in Liver Effective in Pernicious Anemia: I., J. Biol. Chem. **74**:69, 1927.

13. Minot, G. R., and Murphy, W. P.: A Diet Rich in Liver in the Treatment of Pernicious Anemia, J. A. M. A. **89**:759 (Sept. 3) 1927.

Physical Examination.—The infant weighed 5,800 Gm. She was 67 cm. in length. The circumference of the head was 43.4 cm. and of the chest was 37.2 cm. There was a fair amount of subcutaneous fat. The infant was extremely pale, but yellowish discoloration of the skin or mucous membranes did not exist. The musculature was flabby. There was slight craniotabes, and a slight beading of the ribs. The lymph nodes were not enlarged. A loud, blowing, systolic murmur was heard best at the apex of the heart and was transmitted over the entire chest both anteriorly and posteriorly. The abdomen was rounded and tympanitic. The edge of the liver could be palpated 1 cm. below the costal margin, and the spleen

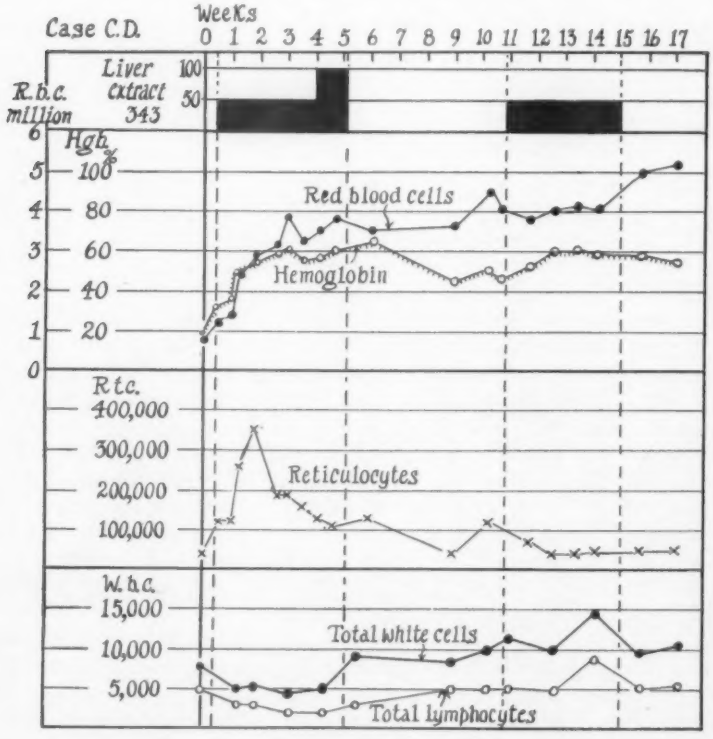

Chart 1 (case 1).—Contrast the striking reticulocyte response during the first period of administration of liver extract with the lack of response during the second period. Note the gradual divergence of erythrocyte and hemoglobin curves after the third week.

In all three charts, the amounts of liver extract 343 are shown in terms of equivalent grains of whole liver.

could be felt at the costal margin. The knee reflexes were normal. Other abnormalities than those noted were not found.

Laboratory Examinations.—At entry, examination of the blood showed 650,000 red cells and 16 per cent hemoglobin (Sahli). There were 8,120 white cells, of which 33 per cent were polymorphonuclears; 57 per cent lymphocytes; 2 per cent eosinophils; 1 per cent basophils; 5 per cent large mononuclears, and

2 per cent transitionals. There was a marked anisocytosis and poikilocytosis, a light polychromasia, and 16 normoblasts to 100 leukocytes, and a few megaloblasts were found. The reticulocytes numbered 7 per cent, or 45,500 in absolute numbers per cubic millimeter. There were 160,000 platelets. The blood counts in the course of observation are shown in chart 1, most of which were done by the same worker.

Urinalysis did not reveal any abnormalities in several specimens. The test for urobilin was negative in three different specimens. The Wassermann test was negative with all antigens on October 13 and 18.

The stool, examined culturally, did not show any *Bacillus welchii,* but did show nonhemolytic streptococci of Brown's gamma type; also bacilli giving the sugar reactions but inconclusive agglutination reactions for Hiss-Russell (Y) dysentery.

A series of roentgenograms of the gastro-intestinal tract after barium did not show any abnormality. The gastric analysis is shown in table 1.

The tests showed an early hypochlorhydria, and later, in spite of the great improvement in the blood picture, they showed a complete absence of free acid and a marked reduction in the output of chloride. The tuberculin test (0.1 mg.

TABLE 1.—*Gastric Analysis*

		Free Hydrochloric Acid	Total Acidity	Chlorides
October 11:				
Fasting		6	20	
After 0.03 mg. of histamine				
Twenty minutes		9	18	
Forty minutes		7	23	
October 26:				
Fasting		0	5	
After 0.05 mg. of histamine				
Twenty minutes		13	35.6	
Forty minutes		0	18	
Jan. 8, 1928:	*pH*			
Fasting	6.4	0	..	0.100 per cent
After 0.1 mg. of histamine				
Ten minutes	6.6	0	..	0.203 per cent
Forty minutes	5.2	0		

intracutaneously) was negative. On October 28, the van den Bergh reactions were negative in the direct test and 0.25 units in the indirect test. The icterus index could not be determined because of hemolysis in the sample. The fragility test was unfortunately not done in this case.

Course.—The use of liver extract (Cohn-Minot fraction) [14] was begun on the second day in the doses and for the periods shown in chart 1. A diet of modified cow's milk, with green vegetables, cod liver oil and orange juice was given throughout the child's stay in the hospital. Whole liver paste (1 ounce) was given on the first day only. There was little regurgitation after the fourth day. Clinical improvement, as shown by improved color, muscle tone and activity, was manifest within a few days, and continued with little interruption. During the period of observation, the infant had several brief periods of fever, none of which, except that due to an intercurrent bronchopneumonia in January, lasted more than twenty-four hours. These occurred on October 6, 10, 15-16, 26-27, December 18-19, 25-26-27, and January 9-10, 13-16 (pneumonia). On each occasion, the temperature

14. Dr. Arthur L. Bloomfield, head of the Department of Medicine, furnished the liver extract used in this case. He obtained a supply from the Committee on Pernicious Anemia of the Harvard Medical School. Arthur G. Dunn made the numerous blood counts in this case.

rose within a few hours to approximately 39 C. (102.2 F.) (rectal), remained up for from six to twelve hours and rapidly returned to normal. Because of some reddening of the tympanic membrane, paracentesis was done during the first of these attacks, but pus was not obtained. The last three attacks were associated with some râles and cough and were probably due to bronchopneumonia. The source of the fever in the earlier attacks is not clear. The infant was dismissed on Nov. 8, 1927, having shown striking clinical improvement. The weight had increased from 5,800 to 7,080 Gm. (nearly 3 pounds) in the five week period. She did well at home, continuing to gain weight, till about December 8, when she developed a cough, not severe, and a severe diaper rash. She was readmitted on December 15. At this time she was a little paler than before and the abdomen was distended, but the physical examination failed to reveal any notable abnormalities other than the still palpable spleen. The fever of December 18-19 was not accompanied by any evidences of inflammation. Liver extract was resumed because of the mild anemia which was still present. The blood picture, however, had changed. The color index was rather low and the anemia was evidently of a secondary type. The reticulocytes were within normal limits and did not show any response to liver extract. Late in this period of liver feeding, the red cell count rose sharply but the hemoglobin, which at first had risen 16 per cent, slightly decreased. The infant made a good and fairly prompt recovery from the pulmonary infection and was dismissed, at the mother's insistence, on January 25.

The chief diagnostic question in this case was whether the condition should be called pernicious anemia or goat's milk anemia of the type described by Brouwer.[15] The child had been fed continuously on goat's milk between the age of 2 years and nearly 10 months. The observations of the blood resembled those of Brouwer's cases, with the exception that there was a leukopenia instead of the leukocytosis which appears to be a constant feature of the latter. Further, the degree of erythropenia (650,000) in this patient is approximately twice as severe as in the lowest of Brouwer's series (1,230,000). The hypochlorhydria and the later achlorhydria in case 1 is a most unusual condition in so young an infant, and forms a striking concordance with the customary gastric conditions in pernicious anemia. The elevation of reticulated red cells (7 per cent) at the time of entry and before treatment had begun was in percentage and not in absolute numbers, which were low. The absence of urobilin from the urine is interesting but does not rule out pernicious anemia. The sudden and marked, but transient, elevation of the reticulocytes may be taken with little question as a response to liver extract. It is extremely interesting to note that while the response to liver, during the first period, was an immediate, rapid and great increase in both red cells and hemoglobin, during the second period the response was different; the red cells rose slightly during the first three weeks and then increased rapidly, while the hemoglobin in the first three weeks increased 16 per cent, and then

15. Brouwer, E.: Ziegenmilch anämie und Ziegenmilchernährung, Jahrb. f. Kinderh. **102**:257, 1923.

gradually fell. The red cells eventually reached normal figures (in the sixteenth week of observation) while the hemoglobin, which reached its peak of 65 per cent in the seventh week, had at the end of observation fallen to 54 per cent. It would appear probable that the sources of stored iron available for the formation of the hemoglobin were exhausted by about the end of the sixth week, and that for some reason little, if any, new iron was being absorbed or made available thereafter.

CASE 2.—*History.*—R. B., a boy, born on Jan. 7, 1928, under supervision at the clinic had been losing weight steadily. The father was 24 years old and was living and well. The mother, aged 23 years, had had vague symptoms of "indigestion" for the last six years, and during pregnancy had had symptoms suggestive but not conclusive, of mild hyperthyroidism. Two months before the patient's birth, the mother's Wassermann reaction had been negative, and the blood had showed: red blood cells, 4,810,000; hemoglobin, 76 per cent (Sahli). Children, born of two previous pregnancies, were living and well. The patient was the second of twins, both boys, with a single placenta and umbilical cord. The birth was easy and without instrumental aid. The first baby weighed 6¾ pounds (3 Kg.) and the second (the patient), 5¾ pounds (2.6 Kg.). The mother had had postpartum thrombophlebitis, which had necessitated hospitalization. The twins were admitted to the hospital as boarders on January 19, when 10 days old.

The mother had been unable to nurse the infants, and the patient, in the twelve days after birth, had lost weight steadily. The weight at birth had been 5 pounds 12 ounces (2.6 Kg.) and the weight on admission was 4 pounds 12 ounces (2.1 Kg.). Vomiting had not occurred, and an average of from four to five good yellow stools had been present daily. There had been a rather persistent oozing of blood from the navel. The right foot had shown from birth a well marked right equinovarus. The examination showed the following abnormalities: poor amount of subcutaneous fat, slightly sunken fontanel, some abdominal distention, a little dried blood on the navel, redundant prepuce and the club foot already mentioned. The color was good. The bleeding time was three minutes; the coagulation time, six minutes. The blood count showed 5,710,000 red blood cells; 88 per cent hemoglobin, and 13,400 white blood cells. The differential count was somewhat peculiar and showed 27 per cent polymorphonuclear neutrophils, 43 per cent lymphocytes, 2 per cent mononuclears, 8 per cent eosinophils, 2 per cent basophils, 14 per cent transitionals and 4 per cent myelocytes. The infant gained rapidly on a suitable formula and was dismissed on February 1, at which time he weighed 2,470 Gm. (5 pounds 7 ounces). The blood counts are shown in chart 2.

The patient was readmitted to the hospital on February 21 because of regurgitation of food, some loss of weight and cough. At this time he weighed 3,180 Gm. The results of the physical examination were negative, but a blood count showed only 3,780,000 red blood cells and 76 per cent hemoglobin—nearly 20 per cent less of each than a month before. It will be noted that the color index was almost 1; a month before it had been 0.76. On a lactic acid formula, the baby gained 210 Gm. in the following eight days and was dismissed. At home, he apparently made normal progress and was not brought back to the clinic till March 31. The night before he had refused his formula and had cried a great deal; at midnight and at 4 and 8 a. m. he had had tonic convulsions lasting about twenty minutes each. That morning his temperature was 102.

The weight at this time was 4,460 Gm.; the skin was slightly yellow; the abdomen was notably distended; the liver was felt 3 cm. below the costal margin; the spleen was palpable, and there was an umbilical hernia. In other respects (excepting the clubfoot), results of the examination were negative. The blood showed an extremely marked reduction in red blood cells and a reduction, though less marked, of the hemoglobin; the color index was then 1.2; and the white cells were moderately increased. Ten normoblasts were seen; there was marked poikilocytosis, anisocytosis and some polychromasia. Three myelocytes were seen. The platelets (two days later) numbered only 80,000. The blood showed a decreased fragility, hemolysis beginning at 0.26 per cent sodium chloride, and was complete at 0.14 per cent. The icterus index was 9.4. The direct van den Bergh test was slightly positive in fifteen minutes (delayed reaction); the indirect test showed 1.5 units. The Wassermann test and the tuberculin test were negative. The contents of the stomach during fasting showed a p_H of 2 (equivalent to

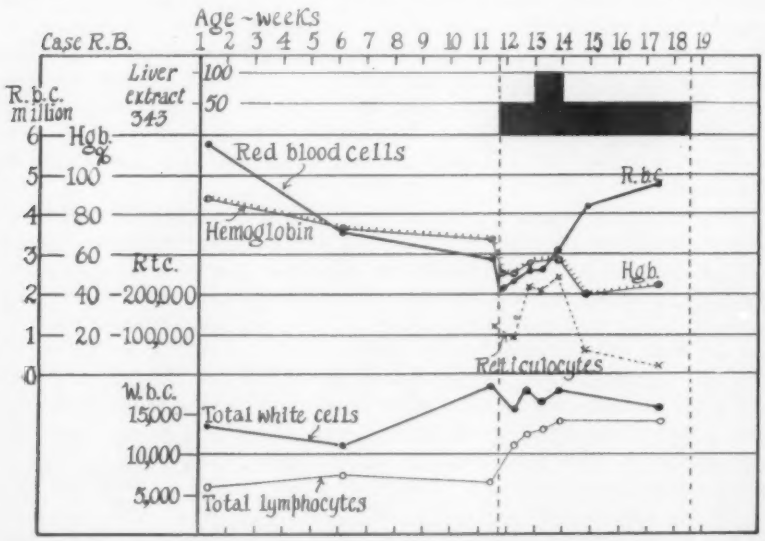

Chart 2 (case 2).—The contrast between the marked increase in erythrocytes during the administration of liver extract and the actual diminution in hemoglobin is well shown. Note also the striking rise in lymphocytes coincident with the administration of liver extract and the corresponding diminution in polymorphonuclear forms. There is well marked reticulocyte response.

10 degrees of tenth normal hydrochloric acid). Neither bile nor urobilin was present in the urine on April 2, the only time at which tests for these substances were made.

The administration of liver extract was begun on April 1, with a daily equivalent of 50 Gm. of whole liver; on April 10, the dose was increased to 100 Gm. equivalent; on April 17, it was reduced to 50 Gm., and was discontinued May 19. Other treatment for the blood was not given. The infant was dismissed from the hospital on April 17, much improved, and weighing 4,840 Gm. The blood had shown a fairly prompt and notable increase in red blood cells, accompanied by a distinct rise in reticulocytes which occurred shortly after the liver extract was begun. The red blood cells continued to increase after the

patient's dismissal from the hospital and had reached approximately normal figures by May 11. The hemoglobin, in sharp contrast to the red cells, failed to rise. The reticulocytes had dropped to normal figures by April 27 and by May 11 had reached the low figure of 0.3 per cent, or a total of about 14,000. Since April 26, the infant had suffered from a mild otitis media from which, at the time this article was written, he was making good recovery.

During each of the hospital periods the infant had had a brief elevation of temperature at irregular intervals. These had occurred on January 19-20 (38 C. or 100.4 F.), 29 (38 C. or 100.4 F.), 31 (38 C. or 100.4 F.); February 24 (38 C. or 100.4 F.); March 31 to April 2 (39 C. or 102.2 F.); April 4 (38 C. or 100.4 F.), and April 11 (38.8 C. or 100.4 F.). None of these attacks could be referred to any discovered source of local inflammation or was accompanied by significant symptoms. The ears were repeatedly examined, and were found normal until April 26. The urine did not contain any pus.

CASE 3.[15]—The first born of the twins, a brother to R. B., weighed 6¾ pounds (3 Kg.) at birth. On January 23 he was admitted to the hospital as a boarder; he weighed 2,760 Gm.. The results of the physical examination were negative; a blood count was not made at that time. He was later watched in the well baby clinic and there he thrived. On April 9, he weighed 13 pounds 6 ounces (6.1 Kg.). At that time the liver was felt 1 cm. below the costal margin, and the spleen was just palpable. A blood count on that day (taken for comparison with the brother) showed 4,160,000 red blood cells; 63 per cent hemoglobin (Sahli), and 12,000 white blood cells. There were 25 per cent polymorphonuclear neutrophils, 4 per cent eosinophils, 25 per cent lymphocytes, 4 per cent large mononuclears, and 4 per cent transitionals. There was a fairly marked anisocytosis and poikilocytosis and basophilia with many stippled red cells, and 1.9 per cent reticulocytes. The next day the baby was returned to the clinic with fever and an acute otitis media, for which he was treated in the ear clinic, and from which recovery was not complete till about four weeks later. It is a matter of regret that, because of family opposition and the difficulties of bringing two infants to the laboratory, it has not been possible to follow the condition of the blood of this child. So far as can be determined, the opportunity has not been given for either child to ingest lead.

In case 2 the high color index, poikilocytosis, anisocytosis, polychromasia, decreased fragility, low platelet count and delayed positive van den Bergh test resemble the conditions in primary anemia. The single incomplete gastric analysis showed free hydrochloric acid; megaloblasts (though many normoblasts were present) were not seen, and urobilin was not found in the urine. The response of the reticulocytes to the administration of liver extract, while not so great in absolute numbers as in case 1, appeared to be typical and definite.

CASE 4.—*History.*—J. S., a boy, born on June 22, 1923, was admitted to the hospital on March 9, 1928, because of pallor and anemia. The parents, aged 31 and 30, were healthy. The mother thought that a few years before examination she might have been anemic. The patient was the first child. There had not been any other pregnancies. The infant was born at eight and one half months; he had weighed 4 pounds (1.8 Kg.) and had been delivered with forceps. The

15. Presented only for comparison with case 2. No liver extract was given in case 3.

infant had been given epinephrine intracardially. He had been breast fed for two months. He had been able to sit up at 8 month of age; cut his first tooth at 9 months, and walked and talked at 14 months. The income of the family, and the housing were fair. The mother said that there was a strong odor of sewer gas from outside the house which frequently made it necessary to close the windows at night. The infant's diet was abundant in vegetables and fresh fruits; he had meat two or three times a week; and an average of 1 quart of milk daily without any tea or coffee. He had not been ill until Dec. 29, 1927.

On December 29, the patient had become extremely tired and sleepy. That night he had had a severe pain in the stomach. A diagnosis of appendicitis was made and the child was operated on the next day. The appendix was said to have been inflamed and there was also a "kink" in the bowel. The recovery was uneventful

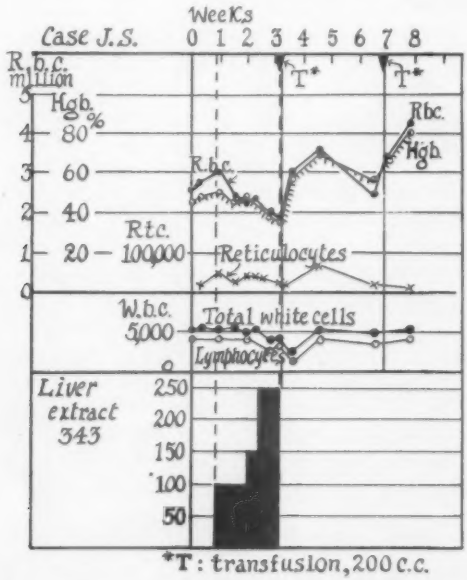

Chart 3 (case 4).—Note the contrast between the failure of liver extract to benefit the anemia with the evident improvement after each of the two transfusions. Reticulocyte response did not occur.

and he went home on the tenth day. Since the operation, however, he has never regained his normal color and has been very pale. About the end of January, 1928, he complained of pain in one elbow and in the upper part of the arm; he protected the extremity and was unwilling to use it. A similar pain occurred in the knees toward the end of Feburary, but was not severe enough to interfere with walking. About March 1, an examination of the blood was made by the private physician who found a severe anemia and referred him to the clinic for treatment.

Physical Examination.—The infant was fairly well nourished, showing marked pallor of the skin and mucous membranes. The skin showed a light yellowish tint, but the sclerae did not suggest discoloration. There were many positive observations: reddened tonsils; moderately enlarged, nontender, cervical glands of the anterior and posterior chains; the liver palpable to 2 cm. below the costal

margin; the spleen palpable to 1 cm. below the costal margin; a healthy appendectomy scar, and incomplete descent of the right testis, which was in the inguinal canal.

Laboratory and Other Tests.—The blood counts were summarized and are shown in chart 3. The following description of a specimen examined on March 15 is fairly representative of the state of the blood up to the time of the first transfusion. The red cells showed a marked variation in size and hemoglobin content. Some were distinctly larger than normal, and some were quite small. About two thirds of the cells showed a marked central pallor, while the remaining cells contained either a normal amount of hemoglobin or an apparently increased amount. A few of the cells were distorted. One typical megaloblast was seen. There was also a moderate polychromasia, and there were several normoblasts. The picture resembled that of a primary anemia.

The Wassermann test was negative, as was the father's. The van den Bergh test, on March 10, showed a negative direct reaction, with an indirect reaction of 0.25 units. On March 27, the direct reaction was negative and the indirect reaction gave 0.15 units. On the latter date, the icterus index was 5.41. Urobilin was not found in the urine on March 9; on March 26, a small amount was present. The stool did not show any abnormalities on March 10; a quantitative

TABLE 2.—*Gastric Analysis*

	p_H	Free Hydrochloric Acid	Total Acidity
Fasting	5.0	0	25
After histamine			
Fifteen minutes	2.8	20	42
Thirty minutes	2.4	25	84
Forty-five minutes	2.6	20	48
Sixty minutes	2.8	14	q.n.s.

measurement of urobilin was not made. The fragility test (March 14) showed hemolysis to begin at 0.26 per cent sodium chloride and to be complete at 0.18 per cent, indicating diminished fragility. The blood belonged to type 4. The tuberculin test (0.1 mg., old tuberculin, intracutaneously) was negative.

Roentgenograms of the urinary tract, spine, pelvis, skull and sinuses did not show any abnormalities.

The gastric analysis gave the results shown in table 2.

Course.—During the first period of hospitalization, from March 8 to April 3, 1928, the boy had three attacks of fever, each lasting about two days, associated with severe pains in the back, radiating to the flanks and down the legs. There was some local tenderness at one time in the costovertebral angles, and spasm of the spinal, lumbar or abdominal muscles; abnormalities of the spine were not determined by the roentgen-ray examination. The urine showed merely a few calcium oxalate crystals at one time and a very few erythrocytes. The dates of onset of these attacks were March 16, 23 and 30. At home, he had another attack on April 16, and during the second period of hospitalization, he had one on April 26, the day after transfusion, which lasted about twenty-four hours. The periodicity of these attacks suggested the possibility of Hodgkin's disease with the relapsing pyrexia of Pel-Ebstein, a diagnosis which we do not yet feel is ruled out. The absence of an increase in the transitional cells, the low normal platelet count and the character of the anemia itself are contrary to the usual conditions in the disease. A mild, atypical relapsing fever due to *Spirillum obermeieri* is another possibility (there have been a few cases recently in Nevada), but spirillums

were not found in blood. Malarial plasmodia were not found. At present, the attacks of fever and pain are without adequate explanation.

During treatment with liver extract, which was carried out for a period of sixteen days with doses increasing from 50 to 250 Gm. of liver equivalent, the anemia steadily increased. This was regarded as a fair trial of the extract. It was, therefore, discontinued on March 30 and a transfusion of 200 cc. of citrated blood was given on that day. An immediate improvement occurred, and the boy was dismissed on April 3. At home, the improvement was maintained, as shown by blood counts taken in the outpatient clinic for about ten days. The next count, on April 23, showed a lower count. The boy therefore, was readmitted for another transfusion, which was given April 25, to the amount of 200 cc., again with immediate improvement. The last count on May 2, showed 4,280,000 red blood cells with 80 per cent of hemoglobin (Sahli). There was a striking improvement in the general condition at this time. The spleen was then barely palpable, and the slight adenopathy had not increased.

There are a number of features in this case which resemble the conditions in pernicious anemia. The appearance of the child with his rather flabby flesh and slight yellowish tint, the enlargement of the spleen, the character of the blood picture, the low red count with high color index, poikilocytosis, anisocytosis, polychromasia, leukopenia, the presence of normoblasts and of megaloblasts, the low reticulocyte count, the increased osmotic resistance of the red cells, the slightly low platelet count and the presence (at one time) of urobilin in the urine were all highly suggestive of primary anemia. The normal gastric secretion is unusual in primary anemia. The pains which were a striking feature of the case, cannot with certainty be traced to neurologic changes; they were not unlike the neuritic pains sometimes seen in pernicious anemia. Irregular fever is, of course, a frequent accompaniment of pernicious anemia, but the fairly regular relapses seen in this case are at least unusual. Everything considered, one might fairly say that none of the observed clinical features and none of the laboratory observations, excepting perhaps the normal gastric production of hydrochloric acid, is incompatible with the diagnosis of primary anemia. Nevertheless, the complete failure of liver extract, 343, given in what appear to be adequate doses suggests that the underlying functional pathologic condition differed from that of the true disease.

Tables 1 and 2 and charts 1, 2 and 3 present the essential features of the examinations of the blood and other special tests before, during and after treatment.

COMMENT

One does not wish to draw far-reaching conclusions from so small a series of cases, nevertheless, certain points are definite enough.

A response to the administration of Cohn-Minot fractional extract of liver, as shown by a prompt elevation of the circulating reticulocytes, red blood cells and hemoglobin and in these respects resembling the

TABLE 3.—*Conditions in the Cases Responding Compared with Those in the Case not Responding to Liver Extract*

Original Observations	Cases Responding to Liver Extract		Case Not Responding to Liver Extract,
	C. D.	R. B.	J. S.
Red blood cells	650,000	2,900,000	2,500,000
Color index*	1.23	1.17	0.90
Nucleated red blood cells	A few megaloblasts; 16 normoblasts per 100 white blood cells	Ten normoblasts; megaloblasts not seen	One normablast (1 megaloblast seen a few days later)
Anisocytosis	Very marked	Marked	Marked
Poikilocytosis	Marked	Marked	Slight
Polychromasia	Marked	Marked	Not noted
Leukocytes	8,120: differential count about normal	17,100: normal differential count, excepting 3% myelocytes	5,200: relative lymphocytosis: 3% myelocytes
Reticulocytes (absolute count)	45,000	120,000	15,000
Platelets	160,000	80,000	190,000
Fragility of red cells	Not tested	Diminished	Diminished
Van den Bergh delayed direct.	Negative	Positive	Negative
Icterus index	Not tested	9.4	5.4
Gastric acidity	Hypochlorhydria; later achlorhydria	Normal	Normal

* The color index has been calculated on the basis of 100 per cent (Sahli) as the normal hemoglobin; some writers consider 80 per cent as normal, which would raise the color index by one fourth.

TABLE 4.—*Character of Response to Liver Extract*

	C. D.	R. B.
Red blood cells	Immediate, rapid rise continuous for first eighteen days of 3,000,000, or 460 per cent of original count; thereafter stationary with minor fluctuations; without effect from second period of administration of liver extract until fourth week, when another increase of about 1,000,000 to normal figures	Immediate, moderately rapid rise continuous for first twenty-two days of 2,100,000, or 100 per cent of original count; thereafter a more gradual rise nearly to normal figures
Hemoglobin	Immediate, rapid rise synchronous with first increase in red cells but lasting about three weeks longer; at the end of this period a total increase of 49, or 300 per cent of original figure; after discontinuance of liver extract, hemoglobin dropped 20 points; during first two weeks of second period of administration of liver extract, hemoglobin increased 13 points, and then gradually fell slightly while the red cells were increasing	A rise of only 6 points during first eight days; thereafter a short stationary period followed by a drop of 16 points and a later slight recovery of 6 points
Color index	Originally 1.23; first less than 1, twelve days after administration of liver extract and thence forward considerably less than 1; at last observation, seventeen weeks after first admission, 0.54	Originally 1.17; over 1 until fifteenth day; after this a very rapid drop to 0.48, at which point it remained for at least two and a half weeks (last count)
Reticulocytes (absolute count)	Maximum, 350,000 on twelfth day of administration of liver extract, thereafter rapid drop to about 100,000 level; this maintained for about six weeks after discontinuance of liver; on resumption of liver, a further drop to 40,000 level	Maximum of 240,000 on fifteenth day; then rapid drop to 60,000 on twenty-sixth day and to 10,000 on fortieth day
White blood cells	Leukopenia during first period of administration of liver; thereafter return to normal figures; with later slight leukocytosis during bronchopneumonia; significant aberration of differential count not present	Leukopenia not present; immediate and rapid rise in lymphocytes, and corresponding drop in polymorphonuclears during first sixteen days of administration of liver; the absolute and relative lymphocytosis persisted to the end of observation, on fortieth day of administration of liver

responses in pernicious anemia as seen in adults, can be obtained in certain cases of anemia during the first year of life.

There does not appear, from the three cases reported, to be any sure criterion by which a response or failure to respond may be predicted, unless a color index above 1 may be so regarded. A color index well over 1 was present in the two cases in which there was a response to the administration of liver extract, while that in the case that did not respond was a little less than 1. The platelet count was lower in the first two cases than in the case in which response did not occur, but in only one instance was it below 160,000. The original level of the reticulocytes in absolute numbers cannot be used as a criterion, neither can the total number of leukocytes, the differential white cell count, the fragility test, nor the gastric acidity be used.

The actual occurrence of true primary anemia in infancy appears to be made more probable by case 1, in which a typical blood picture, a deficiency in acid production in the stomach and a typical reticulocytic response to the administration of liver extract, form a strong chain of evidence. The case of R. B. (case 2), on the other hand, cannot be so regarded, at least if achlorhydria is a sine qua non of diagnosis.

Whether or not the cases here reported are identical with the primary anemia of later life, it is clear that a type of anemia does occur very early in life—and case 2 shows that it may begin at or soon after birth—in which the underlying functional fault is a defective maturation of red blood cells. This type of anemia is readily amenable to treatment with Cohn-Minot fractional liver extract.

Improvement in the blood following the administration of liver extract is shown by an increase in both the red cells and in the hemoglobin. The former, however, evince much greater and more persistent increase than the latter, so that the original picture of primary anemia with a color index well above 1 may be transformed into one of secondary anemia with an index as low as 0.5. That there is some actual stimulation to the increased formation of hemoglobin is suggested by the second period of administration of liver extract to C. D. (case 1), when the hemoglobin rose to a moderate but an apparently significant extent (16 per cent) without a corresponding rise in red cells and without any reticulocyte response whatever.

A marked immediate and persistent increase in the absolute number of circulating lymphocytes, which followed the administration of liver extract in one of the cases, has not, I think, been previously observed. It did not occur in the other two cases. During the period of observation which included two courses of liver extract in large amounts, there was, in case 1, a progressive diminution in the amount of acid secreted by the stomach to a point where free hydrochloric acid could not be demonstrated, even after the administration of histamine. This

phenomenon is, of course, not to be taken as evidence of any deleterious action of the liver extract but as another instance of the well known fact that the achlorhydrias of primary anemia are unaffected by any known means of treatment, and persist even when the blood and general condition are greatly improved.

SUMMARY

1. Three cases of severe anemia in infancy and early childhood with blood pictures resembling that of primary anemia are reported.

2. In two cases—one of an infant, aged 12 weeks and one of an infant, aged 9½ months—a striking clinical and hematologic improvement associated with a characteristic transient rise in the circulating reticulocytes closely followed the administration of Cohn-Minot fractional liver extract.

3. In the third case, that of a boy, aged 4½ years, there was no response of any ascertainable sort to liver extract, and prompt improvement resulted from transfusion of blood.

4. One of the patients, an infant, aged 9½ months, probably had true pernicious anemia, as shown by the blood picture, achlorhydria and typical response to the administration of liver extract. If these criteria are acceptable as conclusive of the diagnosis, this is the earliest authenticated case of pernicious anemia on record.

5. Complete recovery from anemia does not necessarily follow the administration of liver extract, even when a definite response is obtained, since in both infants, who showed such a response, a marked deficiency in hemoglobin persisted after the red cells had reached approximately normal numbers.

6. An increase in the circulating lymphocytes may sometimes occur following the administration of liver extract.

7. Apart from the possibly still debatable question of the occurrence of primary anemia in infancy, there does not appear to be any doubt that as early as the sixth week of human life, a type of anemia does occur in which the maturation of erythrocytes in the bone marrow is defective or inadequate and in which liver extract is of striking therapeutic value.

THE USE OF BISMUTH IN THE TREATMENT OF CHILDREN WITH CONGENITAL SYPHILIS*

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The literature since 1922 has contained numerous reports of the use of bismuth in the treatment of patients with syphilis. A few excellent papers have appeared on the treatment of congenitally syphilitic persons with this drug, but the number of cases reported has been few. Cajal and Spierer [1] were among the first to treat children with bismuth, and in 1923 they reported eight cases in which treatment was administered with favorable results. Belding [2] noted a favorable effect on the Wassermann reaction of the blood in eight children. Beretervide and Thénon [3] reported the use of the drug in twenty-four children, and Bentivoglio [4] in sixteen. Nardi [5] reported on the good results obtained during three years' experience in treating children between the ages of 3 months and 4 years with the drug. Wright [6] recently reported results from the treatment of fifty-four children between the ages of 2 and 10 years; no untoward results were recorded concerning his patients. In 47 per cent of Wright's patients, the Wassermann reactions changed from 4 + to 0.

In view of the meager reports on the use of bismuth in the treatment of children with congenital syphilis, it is thought desirable to report at this time the results in the clinic for syphilitic children in the New Haven Dispensary, where this drug has been used for three and a half years.

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* From the Department of Pediatrics, Yale University, School of Medicine and the Pediatric Service of the New Haven Hospital and Dispensary, June, 1928.

1. Cajal, M., and Spierer, H.: Bismuthothérapie dans la syphilis héréditaire, Presse méd. **31**:354 (April 18) 1923; abstr., Ven. Dis. Inform., Sept. 20, 1923, vol. 4.

2. Belding, D. L.: Wassermann Test: IV. Effect of Bismuth on Wassermann in Patients Unresponsive to Arsphenamine, Arch. Dermat. & Syph. **12**:335 (Sept.) 1925.

3. Beretervide, E. A., and Thénon, J.: Bismuth in Congenital Syphilis, Semana méd. **1**:331 (Feb. 21) 1924; abstr. J. A. M. A. **82**:1307 (April 19) 1924.

4. Bentivoglio, G. C.: Bismuth Treatment of Congenital Syphilis, Riv. di. clin. pediat. (July) 1924; abstr., International Survey of Pediatrics, Sept., 1924, vol. 8.

5. Nardi, G.: Bismuth Therapy in Congenital Syphilis, Riforma med. **41**: 175, 1925; abstr., Ven. Dis. Inform., Nov. 20, 1925, vol. 6.

6. Wright, Carroll S.: Bismuth in the Treatment of Congenital Syphilis, J. A. M. A. **89**:425 (Aug. 6) 1927.

Bismuth was first used in the clinic in November, 1924. Since that time, thirty-one children between the ages of 2 and 12 years have been treated. No case is reported in which the patient was admitted to the clinic after Aug. 30, 1926. The period of observation and treatment is from Nov. 30, 1924, to May 1, 1928.

TECHNIC

The preparation of bismuth used is potassium bismuth tartrate with butyn.[7] The dose is 0.1 Gm., given by intramuscular injection into the buttock, alternate sides being used each week. The same dosage is used regardless of age, since experience has shown that children are relatively more tolerant of bismuth than adults. In using the drug, attention should be given to the following points: 1. In cold weather the ampule must be warmed, not more than one minute, and then shaken, to insure mixing the metallic substance with the oil. In warm weather, merely shaking the ampule may be sufficient. A number 19 Wassermann needle 1¼ inches (3.15 cm.) long is used. 2. The child should lie on the abdomen, with the knees and thighs flexed and the thighs outwardly rotated in order to relax the gluteal muscles. 3. The injection should be made at a point about 1 cm. to the right or left of the intergluteal fold, with the needle pointing outward and downward into the muscle. 4. After the injection is complete, the needle should be disconnected, the plunger pulled back and a small amount (from 2 to 3 cc.) of air injected. 5. After the withdrawal of the needle, the area should be massaged with a sterile gauze sponge. If this technic is carefully followed, the injections are usually nearly painless, and local reactions will not develop.

A course of treatment for syphilis as constituted in this clinic has consisted of: (*a*) six weeks of medication with mercury in the form of daily inunctions of 30 per cent blue ointment (U. S. P.) or weekly injections of mercuric chloride in oil, 1/10 or ¼ grains (0.00648 or 0.162 Gm.) according to age;[8] (*b*) six weeks of arsenic (weekly injections of neoarsphenamine or sulpharsphenamine); six or ten weekly injections of bismuth; (*d*) a rest period of four weeks. If a child has shown any evidence of intolerance to arsenic, the treatment has consisted of a course of mercury alternating with a course of bismuth with a rest period of two weeks between each course. Wassermann tests of the blood are made at the end of each rest period.[9]

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7. From the Dermatological Research Laboratories of Philadelphia, and put up by the Abbott Laboratories of Chicago.

8. One tenth of a grain (0.00648 Gm.) for children under 6 years of age and ¼ of a grain (0.0162 Gm.) for children over 6 years.

9. The serologic examination used is a modified Kolmer test, with icebox fixation. The antigens used are plain and cholesterinized beef heart. The two figures given for the Wassermann reaction indicate the reactions to the plain and to the cholesterinized antigen; for instance, 4-4 would indicate the Wassermann reaction to be 4 + in both antigens; 0-4 would mean Wassermann reaction 0 with plain antigen and 4 + with cholesterinized antigen; 0-0 would mean that the Wassermann reaction was negative in both antigens.

COMPLICATIONS AND REACTIONS

The earlier literature contains references to general and local reactions after the use of bismuth, but as the use of the drug has become more fully understood and proper technic in administration developed, reactions have apparently become less frequent.

Galliot [10] reported a scarlatiniform eruption appearing in a patient after the second injection of bismuth for congenital syphilis. Frank [11] reported the cases of twelve infants treated wtih bismuth, 25 per cent of whom developed "kidney disturbance;" necrosis of the convoluted tubules was found at autopsy on one infant who died. Genoese and Mazzacuva [12] treated infants under 4 months of age, and encountered "transitory toxic symptoms." LeMaire [13] reported one case of jaundice and occasional cases of fever or mild vomiting following the administration of bismuth. A severe stomatitis occurring in a child who was receiving treatment with bismuth has been reported to me from another clinic.[14]

In the administration of bismuth in this clinic, toxic effects have not been encountered. An attempt has been made by cooperation with the dental clinic to have the teeth of syphilitic patients kept clean and to have cavities filled. It is common to see a bismuth line on the gums, especially near the site of a carious tooth or alveolar abscess. A mild gingivitis has occurred occasionally, but severe gingivitis or stomatitis has never been seen. Slight, transitory albuminuria has been found in a few instances, but frank nephritis has not occurred. Treatment has never been interrupted because of any of these observations.

RESULTS OF TREATMENT

In discussing the results of treatment, the thirty-one cases have been divided into five groups. In the first group are seven cases of interstitial keratitis; in the second, four cases of syphilis of the central nervous system; in the third, two cases of arsenic intolerance; in the fourth, nine cases in which the Wassermann reaction was "fixed." Two of the children with syphilis of the central nervous system and the two children with arsenic intolerance also had interstitial keratitis and are discussed in the first group, as well as in the second and third groups. The fifth group consists of thirteen children with latent syphilis who were treated

10. Galliot, A.: Three Cases of Bismuth Erythema, Bull. Soc. franç. de dermat. et syph. **30**:203, 1923; abstr., Ven. Dis. Inform., Jan. 20, 1924, vol. 5.

11. Frank, M.: Bismuth in Congenital Syphilis, Arch. f. Kinderh. **74**:106 (April 5) 1924; abstr., J. A. M. A. **82**:1656 (May 17) 1924.

12. Genoese, G., and Mazzacuva, G.: Bismuth in Hereditary Syphilis, Pediatria **31**:1081 (Oct. 15) 1923; quoted by LeMaire (footnote 13).

13. LeMaire, H.: Le traitement de la syphilis héréditaire du nouveau-né et du nourrison, Nourrison **14**:18 (Jan.) 1926.

14. Personal communication to the author.

with bismuth, arsenic and mercury. This was done in order that the effect of this treatment might be compared later with the treatment of a group of children receiving arsenic and mercury alone.[15]

Interstitial Keratitis.—The only active cases of syphilis in which the patients were treated with bismuth were in this group. In these children, both eyes were affected. The value of any type of general antisyphilitic treatment in acute interstitial keratitis has always been doubtful, and bismuth was used in these cases to determine whether or not the drug was especially effective for lesions of the eye. The children attended the eye clinic, where local treatment of the eyes was carried out. In this group of seven children, five began their antisyphilitic treatment with bismuth. Two children had already been treated with arsenic and mercury. The impression is that the acute symptoms subsided at least as quickly under treatment with bismuth as when arsenic and mercury without bismuth was used. In two cases, there was an almost immediate subsidence of symptoms. The children who were treated with bismuth seem to have recovered with less scarring of the corneas. This group is, however, too small to permit any conclusions to be drawn as to the relative value of bismuth in the treatment of patients with acute interstitial keratitis.

In regard to the Wassermann reaction of the blood, in three cases it changed from 4 + in both antigens to negative, and in all cases it changed to weaker reactions. In the case of one child who was intolerant to arsenic and whose treatment had been limited to mercury and bismuth, the Wassermann reaction after seven courses of bismuth was weakened to 0-4. One child (case 2) in this group had had antisyphilitic treatment before the keratitis developed. She had had two previous attacks of interstitial keratitis and had received four courses of arsenic and mercury, but she had been irregular in attendance at the clinic and there had been periods of months when she had not received treatment. Her Wassermann reaction, however, was 0-4 before the beginning of the treatment with bismuth, but it has become negative and remained so. In spite of this she has recently had a return of keratitis—a fourth attack (table 1).

Syphilis of the Central Nervous System.—Four children who had syphilis of the central nervous system were treated with bismuth. These four children had Wassermann reactions of the blood of 4 +. The Wassermann reaction of the spinal fluid was 4-4 in three and 0-4 in one. The colloidal gold curve was positive in three and negative in one, before treatment with bismuth was begun. Two of the patients had been given treatment with arsenic and mercury before the bismuth was used, without a change in the Wassermann reaction of the blood. Lumbar punc-

15. To be reported later.

tures have been made on only three children after the treatment with bismuth was begun. In one case after one course of treatment with bismuth, the gold curve became negative, but the Wassermann reaction of the spinal fluid was still 4-4. After five courses of bismuth, the Wassermann reaction of both the blood and the spinal fluid became negative. The spinal fluid of the second child was completely negative after the third and fifth courses of bismuth, and the Wassermann reaction of the blood had become 1-4. After the sixth course of bismuth, the Wassermann reaction of the blood was negative. The third child's Wassermann reactions on the spinal fluid and blood were 4 +, and the gold curve was positive after the third course of bismuth (table 2).

TABLE 1.—*Effect of Bismuth Treatment on Wassermann Reaction in Seven Cases of Interstitial Keratitis*

Number	Case Number	Name	Admission Age, Years	First Wassermann	Courses of Arsenic and Mercury	Wassermann Before Bismuth	Wassermann After								
							1 Bismuth Course	2 Bismuth Courses	3 Bismuth Courses	4 Bismuth Courses	5 Bismuth Courses	6 Bismuth Courses	7 Bismuth Courses	9 Bismuth Courses	Last Wassermann	Date of Last Wassermann
1	42859	H. C.	5	4-4	0	4-4	4-4‡	...	0-4*	0-4‡	0-0*	...	...	...	0-0	1/26/28
2	8124	E. D.	12	4-4	4	0-4	0-0†	0-0*	...	...	...	...	...	...	0-0	5/ 2/27
3	47438	M. D.	9	3-4	0	3-4	1-4*	0-0*	0-4	0-4*	0-4*	...	...	...	0-4	3/ 8/28
4	13237	M. M.	5	4-4	4	4-4	0-0	0-0	0-0†	...	...	...	...	...	0-0	1/ 5/28
5	52570	V. S.	8	4-4	0	4-4	1-4	0-4†	0-4‡	0-2	0-3‡	...	...	...	0-3	4/19/28
6	30293	H. T.	9	A-C	0	A-C	0-4	...	4-4†	4-4†	...	...	4-4	...	0-4	4/19/28
7	40087	H. W.	9	4-4	0	4-4	A-C	A-C†	0-3*	A-C*	1-4†	0-0*	0-0*	0-4	0-0	4/14/28
Summary										A-C	4-4	3-4	0-4	0-3	0-0	
First Wassermann										1	5	1	...	...	...	
Wassermann before bismuth										1	4	1	1	...	...	
Wassermann after bismuth										...	...	...	2	1	4	

* Course consisted of bismuth combined with mercury and arsenic.
† Course consisted of bismuth combined with mercury.
‡ Course consisted of bismuth combined with arsenic.

Arsenic-Intolerance.—Two children have had reactions when treated with arsenic, shown by erythema and severe constitutional reactions (fever, vomiting, etc.). One had had four courses of arsenic and mercury previously, and the Wassermann reaction of the blood was still 4-4. While in the hospital with an acute attack of interstitial keratitis, she developed an intolerance to arsenic evidenced by high fever and prostration. After one course of bismuth, her Wassermann reaction became negative. She received two more courses of bismuth, and for the twenty-six months since her last treatment the Wassermann reaction has always been negative in both antigens. In the other case, the treatment has always been limited to mercury and bismuth because of intolerance to arsenic. After nine courses of treatment extending over a period of three years, his Wassermann reaction has become 0-4 (table 3).

TABLE 2.—*Effect of Bismuth Treatment on Wassermann Reaction of Blood and Spinal Fluid in Four Cases of Syphilis of the Central Nervous System*

Blood

Number	Case Number	Name	Admission Age	First Wassermann	Courses of Arsenic and Mercury	Wassermann Before Bismuth	Wassermann After: 1 Bismuth Course	2 Bismuth Courses	3 Bismuth Courses	4 Bismuth Courses	5 Bismuth Courses	6 Bismuth Courses	Last Wassermann	Date of Last Wassermann
1	41849	H. C.	5 yr.	4-4	0	4-4	4-4‡	....	0-4*	0-4‡	0-0*	....	0-0	1/26/28
8	6055	R. H.	3 mo.	4-4	2	4-4	....	0-0*	0-0*	....	....	....	0-0	8/20/27
9	28578	F. L.	8 yr.	4-4	3	4-4	4-4*	....	4-4*	4-4*	....	....	4-4	3/29/28
7	40087	H. W.	3 yr.	4-4	0	4-4	A-C	A-C†	0-3*	0-4*	1-4†	0-0	0-0	4/14/28

Spinal Fluid

Number	Before Bismuth Treatment: Wassermann	Gold Curve	Cells	Globulin	After 1 Bismuth Course: Wassermann	Gold Curve	Cells	Globulin	After 3 Bismuth Courses: Wassermann	Gold Curve	Cells	Globulin	After 5 Bismuth Courses: Wassermann	Gold Curve	Cells	Globulin
1	4-4	3332100000	7	0	4-4	0000000000	§	§	..	.....	..	..	0-0	0000000000	§	§
8	A-C	§	0	§	..	.....	..	..	..	.....	..	..	..	.....	..	..
	1-4	§	150	§												
	0-0	§	2	§												
	0-4	0000000000	11	0												
9	4-4	5553321000	0	0	..	.....	..	..	4-4	2344321000	18	..	..	.....	..	..
7	4-4	2345543100	§	§	..	.....	..	..	0-0	0000000000	§	§	0-0	0000000000	§	§

Summary

	Blood: 4-4	Blood: 0-0	Spinal Fluid: 4-4	Spinal Fluid: 1-4	Spinal Fluid: 0-0	Spinal Fluid: No Record
First Wassermann	4	....				
Wassermann before bismuth	4	....	3	1	....	....
Wassermann after bismuth	1	3	1	....	2	1

	Spinal Fluid: Positive	Spinal Fluid: Negative	Spinal Fluid: No Record
Gold curve before bismuth	3	1	....
Gold curve after bismuth	1	2	1

* Course consisted of bismuth combined with mercury and arsenic.
† Course consisted of bismuth combined with mercury.
‡ Course consisted of bismuth combined with arsenic.
§ No record.

TABLE 3.—*Effect of Bismuth Treatment on Wassermann Reaction in Two Cases Sensitive to Arsenic*

Number	Case Number	Name	Admission Age	First Wassermann	Courses of Arsenic and Mercury	Wassermann Before Bismuth	Wassermann After: 1 Bismuth Course	2 Bismuth Courses	3 Bismuth Courses	4 Bismuth Courses	7 Bismuth Courses	9 Bismuth Courses	Months of Rest	Last Wassermann	Date of Last Wassermann
4	13237	M. M.	5 yr.	4-4	4	4-4	0-0	0-0	0-0†	....	....	....	28	0-0	1/ 5/28
6	30293	H. T.	9 yr.	A-C	0	A-C	0-4	....	4-4†	4-4†	4-4	0-4	..	0-4	4/19/28

Summary:	1 Bismuth Course	4 Bismuth Courses	Months of Rest	Last Wassermann
	A-C	4-4	0-4	0-0
First Wassermann	1	1	....	....
Wassermann before bismuth	1	1	....	....
Wassermann after bismuth	....	....	1	1

† Course consisted of bismuth combined with mercury.

Fixed Wassermann Reaction.—There are nine children whose Wassermann reactions were not changed by routine treatment with arsenic and mercury. The majority of these children have been regular in attendance at the clinic and have had from five to nine courses of treatment. In spite of this, the Wassermann reactions have been persistently positive with complete fixation in both antigens, 4-4. Bismuth was used to determine the effect, if any, on the Wassermann reaction. Also, in view of their prolonged treatment, several of these children have had rest periods, longer than the usual periods of four weeks. Wassermann tests have been made during these rest periods, usually every three months. The result of treatment with bismuth has been a change of the

TABLE 4.—*Effect of Bismuth Treatment on the Wassermann Reaction in Nine Cases of Fixed Wassermann Reactions*

Number	Case Number	Name	Admission Age	First Wassermann	Courses of Arsenic and Mercury	Wassermann Before Bismuth	Wassermann after 1 Bismuth Course	Months of Rest	Wassermann after 2 Bismuth Courses	Months of Rest	Wassermann after 3 Bismuth Courses	Wassermann after 4 Bismuth Courses	Months of Rest	Last Wassermann	Date of Last Wassermann
10	12350	R. B.	9 yr.	4-4	8	4-4	4-4	6	4-4	.	...	...	15	0-4	1/12/28
11	14500	E. C.	8 yr.	4-4	5	4-4	4-4	.	4-4*	3	0-4‡	0-4‡	13	0-4	12/29/27
12	16483	J. C.	7 yr.	4-4	9	4-4	2-4	.	...	.	...	...	17	0-0	6/ 9/27
13	4185	F. D.	9 yr.	4-4	8	4-4	4-4	.	...	.	...	...	24	4-4	12/31/27
14	10353	J. G.	10 yr.	4-4	6	A-C	0-0†	.	0-4*	.	0-4	...	15	0-4	6/ 9/27
15	24306	G. G.	10 yr.	4-4	4	4-4	0-4†	.	0-4*	.	1-4	...	13	0-0	2/ 2/28
16	26949	A. L.	10 yr.	4-4	7	4-4	4-4†	.	A-C†	.	...	...	15	0-4	4/26/28
17	4482	J. M.	17 mo.	4-4	7	4-4	0-4†	.	0-2*	.	0-1*	...	21	0-0	1/ 5/28
18	30603	A. V.	4 yr.	4-4	5	4-4	0-4†	.	0-4*	.	0-0†	0-0	6	0-4	4/12/28
Summary:								A-C		4-4			0-4		0-0
First Wassermann								...		9			...		...
Wassermann before bismuth								1		8			...		...
Wassermann after bismuth								...		1			5		3

* Course consisted of bismuth combined with mercury and arsenic.
† Course consisted of bismuth combined with mercury.
‡ Course consisted of bismuth combined with arsenic.

Wassermann reaction in eight; in three, it became completely negative, and in five 0-4. There is only one child in whom the Wassermann reaction did not change following treatment with bismuth (table 4).

There are thirteen children who have received bismuth as part of their routine treatment. The effect on the Wassermann reaction is shown in table 5. A final report concerning this group of children will be given at a later date, when a comparison will be made with a group of children treated with arsenic and mercury.

SUMMARY

Thirty-one children with late congenital syphilis have received bismuth as part of their antisyphilitic treatment. The effect of the drug has been tried in cases of interstitial keratitis, of syphilis of the central

nervous system, of arsenic intolerance, of fixed Wassermann reactions and in certain other cases.

The effect of bismuth on patients with acute interstitial keratitis seems to have been favorable in the small group treated. The children with syphilis of the central nervous system have shown clinical as well

TABLE 5.—*Effect of Bismuth Treatment on the Wassermann Reaction in the Routine Treatment of Thirteen Cases of Congenital Syphilis*

Number	Case Number	Name	Admission Age	First Wassermann	Courses of Arsenic and Mercury	Wassermann Before Bismuth	Wassermann Reaction After 1 Bismuth Course	2 Bismuth Courses	3 Bismuth Courses	4 Bismuth Courses	5 Bismuth Courses	Last Wassermann	Date of Last Wassermann
19	7922	C. B.	5 yr.	4-4	3	2-4	0-0*	0-4*	0-4‡	0-0	...	0-0	3/ 2/28
20	8317	M. D.	8 yr.	4-4	3	4-4	0-4*	0-3†	0-0‡	0-4	0-4*	0-0	4/17/28
21	50893	C. D.	7 yr.	4-4	1	4-4	0-4*	0-0	...	...	...	0-0	2/ 2/28
22	32623	R. D.	8 yr.	4-4	2	0-0	4-4*	2-4*	4-4	0-4*	...	0-3	4/12/28
23	6727	G. E.	21 mo.	4-4	2	4-4	4-4*	4-4*	A-C	...	...	4-4	4/12/28
24	33052	P. G.	8 yr.	4-4	3	1-4	4-4	...	0-4*	0-4*	0-4‡	0-4	6/30/27
25	25540	L. I.	10 yr.	4-4	1	4-4	4-4*	4;4	4-4†	0-4	...	0-4	4/19/28
26	5301	J. K.	8 yr.	4-4	3	A-C	0-4	0-4*	0-4‡	A-C†	0-2	0-0	3/ 8/28
27	7963	M. K.	6 yr.	4-4	3	4-4	4-4	4-4*	4-4‡	4-4†	...	3-4	3/ 8/28
28	42630	I. M.	11 yr.	4-4	1	4-4	4-4‡	4-4*	4-4*	4-4‡	...	4-4	6/23/27
29	6699	E. P.	9 yr.	4-4	2	4-4	...	4-4*	0-4	0-4*	0-4	0-0	5/10/28
30	19326	S. S.	9 yr.	4-4	3	4-4	2-4†	2-4*	...	...	...	2-4	6/17/26
31	41663	R. S.	9 yr.	2-4	1	2-4	...	0-4*	0-4	0-4†	0-4†	0-4	12/ 1/27

Summary:	A-C	4-4	3-4	2-4	1-4	0-4	0-3	0-0
First Wassermann	...	12	...	1	...	...	...	...
Wassermann before bismuth	1	8	...	2	1	...	...	1
Wassermann after bismuth	...	2	1	1	...	3	1	5

* Course consisted of bismuth combined with mercury and arsenic.
† Course consisted of bismuth combined with mercury.
‡ Course consisted of bismuth combined with arsenic.

TABLE 6.—*Summary Showing the Effect of Bismuth Treatment on Wassermann Reaction in Thirty-One Cases of Congenital Syphilis*

	A-C	4-4	3-4	2-4	1-4	0-4	0-3	0-0
First Wassermann	1	28	1	1	...	...	...	...
Wassermann before bismuth	3	21	1	3	1	1	...	1
Wassermann after bismuth	...	4	1	1	...	10	2	13

First Wassermann positive (4-4, 3-4, 2-4)	31 children	100%
After bismuth treatment, Wassermann positive (4-4, 3-4, 2-4)	6 children	19%
After bismuth treatment, Wassermann negative (0-0)	13 children	42%
After bismuth treatment, Wassermann negative partially (0-4)	10 children	32%
After bismuth treatment, Wassermann negative partially (0-3)	2 children	7%

as serologic improvement. The most valuable use of bismuth is in the treatment of children who are intolerant to arsenic. Bismuth has been sufficiently effective in changing fixed Wassermann reactions to make its use indicated in these cases. A summary of the effect of treatment with bismuth on the Wassermann reactions of the blood is shown in table 6.

Bismuth is valuable in the treatment of patients with congenital syphilis. It is a drug which is well tolerated by most children.

SUBACUTE BACTERIAL ENDOCARDITIS IN CHILDHOOD

REPORT OF TWELVE CASES *

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The first clinical description of this disease was reported by Kirkes.[1] However, Corvisart and Leroux,[2] in 1801, were the first to describe vegetations on the valves and the wall of the auricle which appeared to be typical of those of subacute bacterial endocarditis. In 1810, Wells [3] described similar lesions. Since then, a great many cases in adults and comparatively few cases in children have been reported from various clinics in Europe and in our own country. In 1869, Bouchut [4] gave a classic description of the pathologic changes in a child, aged 8 years, who died of a cerebral embolus. Harbitz [5] and Litten [6] gave the earliest satisfactory description of the pathologic anatomy and histology. During the past twenty-five years, a far greater appreciation of this disorder has become manifest by the ever increasing studies and reports of such observers as Koeniger,[7] Loehlein [8] and Gaskell [9] whose great interests were in the pathologic aspect, while Schottmüller,[10] Rosenow,[11] Horder [12] and others contributed mainly to the study of the bacteriology of this malady. Excellent clinical contributions were made by Osler,[13]

* Received for publication, June 29, 1928.

* From the Pediatric Service of Dr. Bela Schick, Mount Sinai Hospital.

1. Kirkes, W. S.: M. Chir. Tr. **35**: Sec. Ser. 281, London, 1852.

2. Corvisart, J. N., and Leroux: A Treatise on the Diseases and Organic Lesions of the Heart and Great Vessels, J. de med. chir. et pharm. **1**:99, 1801.

3. Wells, W. C.: On Rheumatism of the Heart, Transactions of a Society for the Improvement of Med. and Chir. Knowledge, London **3**:373, 1812.

4. Bouchut: Des Embolies du cerveau chez les enfants et de leur diagnostic par la cérébroscopie, Gaz. d. Hôp., no. 60, pp. 233 and 241, May 27 and June 17, 1869.

5. Harbitz, F.: Deutsche med. Wchnschr. **15**:121, 1899.

6. Litten, M.: Berl. klin. Wchnschr. **36**:609 and 644, 1899.

7. Koeniger, H.: Arb. a. d. path. Inst. Leipzig, 1903, vol. 2.

8. Loehlein, M.: Med. Klin. **6**:375, 1910.

9. Gaskell, J. F.: Proc. Roy. Soc. Med. **7**:109 (Path. Sec., March 17) 1914.

10. Schottmüller, H.: München. med. Wchnschr. **57**:617, 1910.

11. Rosenow, E. C.: J. Infect. Dis. **6**:245, 1909; **7**:411, 1910.

12. Horder, T. J.: Tr. Path. Soc. London **57**:58, 1906; **58**:265, 1907; Brit. M. J. **2**:301, 1920; Quart. J. Med. **2**:289, 1908-1909.

13. Osler, W.: Malignant Endocarditis (Goulstonian Lectures), Brit. M. J. **1**: 467, 522, 577, 1885.

Billings,[14] Jochmann,[15] Kastner [16] and others. We cannot conclude this brief historical review without paying especial tribute to Libman [17] and his co-workers for the many careful, painstaking and accurate observations on the bacteriology, pathology and clinical features of this disorder. Their studies, however, were conducted mainly on adults.

Observations on children under 14 years of age are rather scarce in the literature. One rarely finds the condition mentioned in American or foreign textbooks on pediatrics, and a review of the literature of the past half century listed only sixty-four cases in children. Many cases cited by different authors did not, in our opinion, warrant the inclusion under the heading of subacute bacterial endocarditis. While it is true that many cases which we included did not show a positive blood culture, they did show petechiae, an enlarged spleen, cerebral involvement, a characteristic course or a typical condition post mortem. Blumer [18] and Neto [19] have written extensive monographs and include a comprehensive review of the literature. There were a number of case reports of aneurysm and embolism in children which were in reality definite cases of subacute bacterial endocarditis.

INCIDENCE

We have been unable to find reliable figures as to the age incidence of this disorder in childhood. Horder, in reporting 88 cases including adults and children, stated that 10 per cent were in children under 15 years. The exact age incidence is not given. In his review of 317 cases, Blumer included Horder's series. He stated that one patient was under 10 years and that fifty-four were between 11 and 20 years. His analysis was based only on instances in which there was available an actual case history which could be studied and analyzed. Blumer,[20] however, has seen several definite cases since the publication of his monograph. In Libman's [21] first 149 personal cases of subacute bacterial endocarditis, only one occurred in a child under 10 years of age. Tables 1 and 2 give the age incidence in the case reports which we collected from the literature and of our own series of 12.

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14. Billings, F.: The Practical Medicine Series, Chicago, Year Book Pub. Co., 1921, vol. 1, p. 224.
15. Jochmann, G.: Lehrbuch der Infektiose Krankheiten, Berlin, 1914.
16. Kastner, A.: Deutsches Arch f. klin. Med. **126**:170, 1918.
17. Libman, E.: Bull. Johns Hopkins Hosp. **17**:215, 1906; Proc. New York Path. Soc. **11**:118, 1911; Am. J. M. Sc. **144**:313, 1912; **146**:625, 1913; M. Clin. N. Amer. **2**:117, 1918; Brit. M. J. **2**:304, 1920. Libman, E., and Celler, H. L.: Am. J. M. Sc. **140**:576, 1910.
18. Blumer, G.: Medicine **2**:2, 1923.
19. Neto, J. M.: Thèse Sao Paolo, 1926.
20. Personal communication to the authors.
21. Personal communication to the authors.

In the two series in the tables, we do not encounter any instance of the disease before the age of 5. This would tend to bear out our contention that the cases reported before the fifth year, unless proved at postmortem examination or bacteriologically during life, must be analyzed critically. We are not including in our report cases of acute bacterial endocarditis of varying etiology as these differ pathologically from the typical cases of subacute bacterial endocarditis. There are many references to cases of congenital cardiac disease in which a fresh infective endocarditis was found post mortem. This is especially true in Lewis and Grant's [22] series of cases of bicuspid aortic valves on many of which there was a superimposed infection. Most of these cases occurred in adults.

The twelve cases representing our series have been studied during the past ten years, and it is not unlikely that a number may have escaped

TABLE 1.—*Age Incidence in Cases from the Literature* *

Age in years	1	2	3	4	5	6	7	8	9	10	11	12	13
Number of cases	0	0	0	0	5	2	7	9	6	5	14	7	6

* Osler reported three cases in children under 10 years of age, the exact age not being given.

TABLE 2.—*Age Incidence in Twelve Cases from the Pediatric Service of Mount Sinai Hospital*

Age	Cases	Age	Cases
1 to 5 years	0	9 years	1
6 years	1	10 years	2
7 years	0	11 years	2
8 years	3	12 years	3

our notice or the patients may have left the hospital before a careful study could be made and a definite diagnosis established. Perhaps some were in the bacteria-free stage, and the condition could not be so readily diagnosed. A more intimate knowledge of the symptoms and signs of this disorder will undoubtedly enable us to recognize these cases more readily.

ETIOLOGY

All statistics show that rheumatic fever is the chief predisposing factor in the development of subacute bacterial endocarditis. Because of the insidious nature of the onset of rheumatic fever, it is not unlikely that many cases of subacute bacterial endocarditis for which there is no definitely known predisposing cause are nevertheless of rheumatic origin.

22. Lewis, T., and Grant, R. T.: Observations Relating to Subacute Infectious Endocarditis, Heart **10**:21, 1923.

One often obtains a history of "growing pains" or of tonsillitis in childhood, which may be rheumatic manifestations. Infected teeth and sinuses may also play a rôle. Congenital cardiac disease in a small percentage of cases is responsible for the development of subacute bacterial endocarditis in childhood.

In our series, there was a definite cardiac or rheumatic history in ten of twelve cases and of scarlet fever complicated by arthritis in one. In two cases there was no history of any previous disease. None of the twelve patients in our series had had chorea. In only three reported instances in children had there been chorea previously. Congenital cardiac disease was present in one case of our series (case 7). It was given as an etiologic factor in five of the sixty-four case reports which we collected from the literature. Blumer (personal communication) also has observed a few cases since the publication of his monograph.

BACTERIOLOGY

Lenhartz,[23] Libman and Schottmüller were among the first to associate nonhemolytic streptococci with subacute bacterial endocarditis. They found that these organisms grew readily on blood agar plates. In the present series, nonhemolytic streptococci were obtained from cultures of the blood in nine cases, and *B. influenzae* in one. The streptococci belonged to the α and γ type of Brown [24] and were isolated on blood agar plates on one or more occasions, many colonies per cubic centimeter always being found.

PATHOLOGY

The condition found post mortem in this disease has been thoroughly described by Harbitz, Litten, Libman and others, and does not need further elucidation by us except the statement that in children the characteristic manifestations of the endocardial lesions engrafted on an old endocarditis or a congenital cardiac lesion and the embolic phenomena (splenic, cerebral, pulmonary and kidney) are identical with those found in adults. Mycotic aneurysm has also been found. The focal embolic glomerular lesions were first described by Loehlein and later by Baehr [25] and Gaskell. The "flea-bitten" kidney (Guy's Hospital) is characteristic also in children.

GENERAL SYMPTOMATOLOGY

Because of the extreme variability of the clinical manifestations, it is difficult to describe a definite composite picture. We will therefore

23. Lenhartz: München. med. Wchnschr. **48**:1123 and 1178, 1901.

24. Brown, J. H.: Rockefeller Inst. Monograph no. 9, 1919.

25. Baehr, G.: Significance of Embolic Glomerular Lesions of Subacute Streptococcus Endocarditis, Arch. Int. Med. **27**:262 (Feb.) 1921.

confine ourselves to the general symptomatology only, emphasizing certain salient points which we have found particularly helpful.

The early manifestations may be those of a low grade toxemia with an insidious onset, the patient complaining of lassitude, anorexia, pains in the extremities, which are fleeting at times, feverishness, chilliness, headache and occasionally cardiac discomfort. The onset may be more abrupt and acute with high fever, chills and sweats. Later, pallor and curious pigmentation (café au lait) of the skin, particularly of the face, and emaciation are present. Tenderness of the lower sternum, clubbing of the fingers and toes, and swelling of the joints occur, and, as the disease progresses, embolic phenomena appear, such as petechiae (white centered) on the conjunctivae, face or upper portion of the chest. Abdominal pain, which occurs most frequently in the left hypochondrium, splenic tenderness and enlargement of the spleen and liver are frequently present. Tender nodules about the pads of the hands, fingers and toes (Osler nodes) are pathognomonic except for their rare occurrence in cases of atypical verrucous endocarditis (Libman and Sacks [26]). Cerebral lesions evidenced by sudden loss of consciousness, hemiplegia, muscular twitchings, facial and ocular palsies, sudden blindness due to embolism of the central artery of the retina and sudden pulmonary infarction may also occur. There may be precordial discomfort due to cardiac involvement. Melena occurs in certain cases. Gangrene of an extremity due to obliteration of an artery by an embolus has also been described. Occasionally when petechiae are not found in the skin, retinal hemorrhages may be present and may therefore be a valuable diagnostic sign.

DURATION AND TERMINATION

The duration of this malady varies. It depends on the virulence of the infection and the general condition of the patient. Many cases present frequent remissions with marked general improvement and may become mild for weeks or months, and then become active again and in a short time the patient may die suddenly. In many it is difficult to determine the date of onset, so that we can base our opinion as to the duration of the case only from the time that it first was studied. Because of the insidious onset, one can readily appreciate the inaccuracy of the stated duration in a large group of cases. Blumer and Libman stated that patients have lived as long as eighteen months or even two and one-half years. Libman also called attention to the fact that occasionally in patients with subacute bacterial endocarditis the condition actually heals and life expectancy is great.

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26. Libman, E., and Sacks, B.: A Hitherto Undescribed Form of Valvular and Mural Endocarditis, Arch. Int. Med. **33**:701 (June) 1924.

The cause of death in our series was most often cerebral embolism. Some patients succumb as a result of cardiac and renal insufficiency and some as the result of an intercurrent or terminal infection.

DIAGNOSIS

In our opinion, it is of primary importance to bear in mind the fact that subacute bacterial endocarditis does occur in childhood, and that because of the protean character of this disorder, it may simulate other diseases.

The cardinal diagnostic features are fever, white centered petechiae on the conjunctivae, mucous membranes of the oral cavity, chest and inner aspect of the arms and on the sides of the neck, splenic enlargement, pain and tenderness in the left hypochondrium and an organic cardiac murmur. Other features are the tender Osler nodes on the pads of the fingers and toes, the café au lait color and the clubbing of the fingers. The finding of large mononuclear cells, the so-called macrophages or histiocytes, in a blood smear taken from the lobe of the ear, the presence of red blood cells in the urine and finally the isolation of a nonhemolytic streptococcus from the blood stream are valuable laboratory aids. A positive blood culture may not always be present either because there are bacteria present in the blood stream which will not grow on the mediums used or else because the patient is in the healing or bacteria-free stage. We have had two cases in which repeated blood cultures were negative. In one of these (case 7), post-mortem investigation corroborated our clinical diagnosis. In the second case (case 12), permission for necropsy unfortunately could not be obtained, but the clinical evidence was unquestionable.

In patient's with subacute bacterial endocarditis, the condition is most frequently overlooked because of its apparent similarity to that of rheumatic endocarditis. Certain characteristics, however, are distinctly different in the two conditions. In none of our cases were subcutaneous tendinous nodules present. They have been reported in the literature in only one instance, but in that case a mixed infection was probably present. In rheumatic fever, on the other hand, nodules are frequently present.

The spleen was palpable in nine of our twelve cases, whereas the infrequency of this condition in rheumatic fever is striking. Fibrinous pericarditis during the course of subacute bacterial endocarditis is rare. In rheumatic fever, a large percentage of cases show clinical evidence of such involvement.

The patient suffering from subacute bacterial endocarditis often looks well in contrast to the rheumatic patient, because there is less involvement of the myocardium and usually decompensation is not present. Auricular fibrillation did not occur in our series. Chills occurred in one

TABLE 3.—*Summary of the Outstanding Data in Our Series*

Name	Age	Previously Known Valvular Disease	Range of Fever	Hematuria	Petechiae	Embolic Pneumonia	Blood Counts	Blood Chemistry	Blood Culture	Termination
1. I. G.	10	—	98-104 F.	+	+	Cerebral	Leukocytes.....10,600 Polymorphonuclears..88% Lymphocytes.....12%	Not done	Nonhemolytic streptococcus	Died; no necropsy
2. J. M.	8	+ 6 years	98-103 F.	+	+	Renal	Leukocytes.....12,000 Polymorphonuclears..80% Lymphocytes.....20% Erythrocytes.....1,700,000 Hemoglobin.....28%	Urea.....60.2 Nonprotein nitrogen...78.5 Uric acid..... 3.8 Creatinine..... 1.8 Cholesterol..... 0.136	B. influenzae	Died; no necropsy
3. A. G.	12	+	98-103 F.	—	+	Splenic	Leukocytes.....18,000 Polymorphonuclears..88% Lymphocytes.....12%	Not done	Nonhemolytic streptococcus	Died; no necropsy
4. L. P.	9	+	100-102 F.	+	+	Renal	Leukocytes.....21,000 Polymorphonuclears..95% Hemoglobin.....62% Erythrocytes.....3,760,000	Not done	Nonhemolytic streptococcus	Died; necropsy
5. N. H.	11	—	98-103 F.	+	+	Mycotic aneurysm abdominal aorta	Leukocytes.....34,000 Polymorphonuclears..88% Lymphocytes.....12%	Urea.....16.8 Nonprotein nitrogen...43.1 Uric acid ..... 3.2 Creatinine..... 2.5 Cholesterol..... 0.296	Nonhemolytic streptococcus	Died; no necropsy
6. A. W.	8	+ 3-4 years	98-103 F.	+	+	—	Leukocytes.....9,000 Polymorphonuclears..65% Lymphocytes.....35%	Not done	Nonhemolytic streptococcus	Died; no necropsy
7. G. M.	12	+ 3 years	None for weeks after admission	+	+	Splenic	Leukocytes.....4,200 Polymorphonuclears..61% Lymphocytes.....39% Erythrocytes.....2,690,000 Hemoglobin.....45%	Urea.....16.8 Nonprotein nitrogen...49.0 Uric acid..... 2.7 Creatinine..... 1.3 Cholesterol..... 0.208	Negative during life; nonhemolytic streptococcus from valves at necropsy	Died; necropsy
8. M. S.	8	+ 3-4 years	99-104 F.	+	+	Splenic and cerebral	Leukocytes.....10,300 Polymorphonuclears..76% Lymphocytes.....24% Erythrocytes.....3,700,000 Hemoglobin.....47%	Urea.....16.0 Nonprotein nitrogen...35.0 Uric acid..... 1.5 Creatinine..... 1.5 Cholesterol..... 0.118	Nonhemolytic streptococcus	Died; no necropsy
9. H. K.	6	Frequent ? attacks of rheumatism	99-103 F.	+	+	Splenic	Leukocytes.....10,000 Polymorphonuclears..80% Lymphocytes.....20% Erythrocytes.....4,000,000 Hemoglobin.....65%	Not done	Nonhemolytic streptococcus	Dying when discharged
10. J. H.	12	+ 3 years	99-104 F.	+	+	Splenic and hepatic	Leukocytes.....8,000 Polymorphonuclears..82% Lymphocytes.....18%	Urea.....14.0 Nonprotein nitrogen...34.1 Uric acid..... 2.8 Creatinine..... 1.0	Nonhemolytic streptococcus	Died; necropsy
11. M. H.	10	+ Scarlet fever arthritis at 5 years	99-104 F.	+	+	Cerebral	Leukocytes.....13,200 Polymorphonuclears..72% Lymphocytes.....28% Erythrocytes.....3,870,000 Hemoglobin.....28%	Not done	Nonhemolytic streptococcus	Died; necropsy
12. J. S.	11	+ 2 years	99-104 F.	—	+	Splenic	Leukocytes.....16,400 Polymorphonuclears..71% Lymphocytes.....29% Erythrocytes.....4,000,000 Hemoglobin.....67%	Urea.....17.0 Uric acid..... 3.0	Negative	Died; no necropsy

case. White centered petechiae are not present in cases of rheumatic fever but were present in all of our twelve cases. Hematuria is usually present in subacute bacterial endocarditis and is rare in rheumatic fever.

PROGNOSIS

In general, it may be stated that the prognosis is extremely grave. Most patients die after from four months to two and a half years from the time the disease is diagnosed. Isolated instances of recovery have been reported, but we did not have any in our series.

THERAPY

Many forms of therapy have been tried, including vaccines, arsenical preparations, serums and transfusion of blood, without any permanent benefit. Our main hope at present lies in prophylaxis. All possible foci of infection should be eradicated. The general health and resistance to infections should be built up by proper diet and hygiene. If feasible, changes in environment should be recommended, particularly during the season of the year when infections of the upper respiratory tract are prevalent. This should particularly apply to the chronically cardiopathic child, who should be under constant careful supervision.

REPORT OF CASES

CASE 1.—*History.*—I. G., a boy, aged 10 years, was admitted to the hospital on Oct. 24, 1916, and died on Feb. 3, 1917. There was no previous history of rheumatism, scarlet fever or tonsillitis. The present illness began three weeks before admission, with fever, general malaise, nausea and for the last three days, sharp pain in the left side of the chest.

Physical Examination.—Pallor, no petechiae, dulness over both lower lobes, râles and diminished breath sounds, double mitral and aortic lesions, marked Corrigan pulse and pulsation in the neck were present. The tonsils were not enlarged. The spleen was palpable 2 cm. below the costal margin but was not tender. Neurologic signs were not present. The temperature was 100 F. on admission and later ranged between 98 and 104; it was of the hectic type.

On October 16, examination of the blood showed: leukocytes, 10,600; polymorphonuclears, 88 per cent; lymphocytes 12 per cent.

On October 21, the leukocytes numbered 12,100, the polymorphonuclears, 77 per cent and lymphocytes, 23 per cent.

Course of Illness.—On November 3, there was a slight hemiplegia on the right side; on November 14, there was considerable improvement. On November 17, petechiae were first noted in the conjunctivae. On November 24, acute swelling and pain were present in the left ankle. On January 10, the toes and soles of the feet were tender. Blood cultures were positive for *Streptococcus anhemolyticus* on November 3, December 4 and January 11 on solid mediums. The urine was examined repeatedly and showed a trace of albumin, a few hyaline casts and red and white cells. Blood chemical determinations were not made. The child died in decompensation. Necropsy was not permitted.

CASE 2.—*History.*—J. M., a boy, aged 8 years, was admitted to the hospital, Aug. 24, 1917, and died, Sept. 19, 1917. He had had chronic cardiac disease for six years with fever, pallor, precordial pain and dyspnea, which intermittently confined him to bed. He had not had scarlet fever, chorea or rheumatic fever. For the past seven weeks, he had been having pain in the feet, precordial pain, edema of the face and increasing pallor.

Physical Examination.—Bilateral hydrothorax, enlarged heart, a mitral lesion, ascites, palpable liver and spleen and edema of the scrotum and feet were present. On October 24, petechiae were present. The skin was a café au lait color. On October 25, examination of the blood revealed: leukocytes, 12,000; polymorphonuclears, 80 per cent; lymphocytes, 20 per cent; erythrocytes, 1,700,000, and hemoglobin, 28 per cent. On October 31, the number of petechiae had increased. The hemoglobin was 19 per cent. Several transfusions were done. The urine showed: specific gravity, from 1.018 to 1.020; albumin + +; numerous hyaline casts; numerous leukocytes and occasional erythrocytes. Blood chemical determinations showed: urea, 60.2; nonprotein nitrogen, 78.5; uric acid, 3.8; creatinine, 1.8; cholesterol, 0.136. On September 7 and 10, blood culture was positive for *B. influenzae*. The excretion of phenolsulphonphthalein was 15 per cent in two hours.

Course of Illness.—On September 11, large ecchymoses were found on the abdomen and chest. The temperature ranged from 99 to 103 and was of the hectic type. Several transfusions of blood were given, but without any sustained benefit. This was a case of terminal decompensation in subacute bacterial endocarditis, probably with involvement of the kidneys. Necropsy was not permitted.

CASE 3.—*History.*—A. G., a boy, aged 12 years, was first admitted to the hospital on Nov. 3, 1918. He went home against advice on Nov. 20, 1918.

The past history was unimportant, except for an attack of rheumatism when he was 4 years old. The child was supposed to have had an attack of influenza recently and had continued to cough and have fever thereafter. The present illness had begun six days before admission to the hospital with sharp pain in the right lower quadrant of the abdomen but without vomiting. A diagnosis of appendicitis (?) was made on admission.

First Physical Examination.—The tonsils were large and cryptic; the heart was enlarged, with systolic and diastolic murmurs; the pulse was of the Corrigan type. The abdomen was not enlarged, and rectal examination revealed nothing of importance.

Course of Illness.—The child was not operated on. On November 4, slightly raised erythematous patches about the size of a dime, which felt warm to the touch and were slightly tender over both outer condyles of the femur and the left internal malleolus, were present. On November 8, the erythema was gone and no petechiae were present. The leukocytes numbered 18,000; the polymorphonuclears, 88 per cent; lymphocytes, 12 per cent. The temperature on admission was 103. Lysis occurred in eight days. On November 18, irregular rises in temperature up to 102 occurred. On November 9, blood culture was negative. On November 18, blood culture was positive for *Streptococcus anhemolyticus.* The urine showed: no albumin and an occasional leukocyte and granular cast. Blood chemical determinations were not made.

This patient was not seen again until 1921, three years later, when he was admitted to the cardiac clinic. He was now 15 years old and had had frequent attacks of chills and fever which had been diagnosed as malaria at home. He had become weak, tired, dyspneic and ran a continued low grade, afternoon fever.

Second Physical Examination.—The child was poorly nourished and pale; the tonsils were enlarged; petechiae were present over the right side of the neck and the left axilla; marked carotid pulsations were felt; the precordium was heaving; the heart was enlarged to the left and the right, with a systolic murmur at the apex and systolic and diastolic murmurs at the base; the edge of the spleen was palpable; marked tenderness and swelling were present over the right index and right fifth finger tips and the right great toe (Osler nodes). The boy had frequent attacks of pain in the left side of the abdomen below the costal margin (probably splenic infarction). In July, 1921, he was mentally confused and dizzy and had severe headache.

He was readmitted to the hospital in July, 1921.

Third Physical Examination.—Pallor; a temperature of from 100 to 104 daily; petechiae over the upper part of the chest; loud murmurs, especially over the base of the heart, and a dilatation of the aorta seen in a roentgenogram, due either to a dilatation of the aorta or pulmonary artery or to a mycotic aneurysm of one of these vessels were present. The blood count showed: hemoglobin, 65 per cent; erythrocytes, 3,100,000; leukocytes, 15,200; polymorphonuclears, 75 per cent; lymphocytes, 24 per cent; monocytes, 1 per cent. Blood cultures showed 250 colonies of *Streptococcus anhemolyticus* per cubic centimeter. Urine showed albumin + and an occasional erythrocyte.

Course.—The boy was removed from the hospital against advice and died at home several days later. This case may have been one of rheumatism on the first admission, in view of the clinical manifestations and the organism that was found in the blood. On the second admission, the patient had, however, a subacute bacterial endocarditis, which was confirmed by the finding of 250 colonies of *Streptococcus anhemolyticus* per cubic centimeter in the blood culture. The date of onset of the subacute bacterial endocarditis cannot be accurately determined.

CASE 4.—*History.*—L. P., a girl, aged 9 years, was admitted to the hospital on Dec. 25, 1919, and died the same day.

She had been in Mount Sinai Hospital in April, 1915, at the age of 3½ years. At that time she complained of pains in both feet, cardiac palpitation, dyspnea and vomiting. She had enlarged tonsils; a systolic murmur was heard over the precordium; the edge of the liver was palpable; the temperature ranged from 99 to 100. The urine showed a trace of albumin, and a few hyaline casts, erythrocytes and leukocytes. The pulse rate ranged from 120 to 140 on admission and later fell to from 88 to 92. The diagnosis was rheumatic endocarditis. Following this attack, she remained in fairly good health until three weeks before the present admission, when she had irregular fever, lost weight, had precordial pain and headache, and a few days before admission, sudden pain in the right shoulder and in the right upper quadrant of the abdomen. Suddenly, just before admission, the child became unconscious and a right hemiplegia was noted.

Physical Examination.—The child was in a stupor and was pale; petechiae were present on the eyelids, uvula and buccal mucosa, and presystolic and systolic murmurs were heard over the cardiac apex; the edge of the liver was palpable, but the spleen was not felt. The blood count showed: hemoglobin, 62 per cent; erythrocytes, 3,760,000; leukocytes, 21,000 and polymorphonuclears, 95 per cent.

Course of Illness.—The child did not recover consciousness and died within eight hours after admission. Blood culture taken on admission was positive for anhemolytic streptococci. The temperature ranged from 100 to 102 before death.

Necropsy.—Enlargement of the heart, a normal pericardium, a moderately dilated right ventricle and vegetations on the auricular wall and the mitral valve

were found. The spleen was twice the normal size without infarcts. Cultures of the spleen made post mortem were negative. Crushings from vegetations on the valves showed gram-positive cocci. There was an infarct of the right kidney, and about one glomerulus in ten showed a characteristic embolic lesion. Some were old and hyalinized and at least two were fresh. The lungs showed an occasional area of purulent bronchopneumonia. The liver showed some enlargement with cloudy swelling. The pathologic diagnosis was subacute bacterial endocarditis.

CASE 5.—*History.*—N. H., a girl, aged 11½ years, was admitted to the hospital on May 14, 1920, and died on June 22, 1920. She had had pneumonia six years before admission. Later, she had been told that she had heart trouble, but she did not have any symptoms of cardiac disease. The exact onset of the cardiac disease is not known. She had not been confined to bed at any time; she had not had dyspnea and had continued her duties without interruption.

The present illness had begun rather abruptly five weeks before admission, when she had had a rash on the legs and pains in the extremities. She had had intermittent fever for two weeks before admission. One week before admission, pain of a few days' duration had been present in the right flank. She had also had pain in the left foot for one day and sharp pain in the right shoulder for one week. She had had slight headache and blurring of vision at varying intervals for five weeks and had been nauseated during that time. Her temperature had been as high as 102 F.

Physical Examination.—Petechiae were present on both palpebral conjunctivae and also on the skin below the left clavicle; the tonsils were enlarged; systolic and diastolic murmurs were heard over the precordium and also posteriorly; the spleen and kidneys were not palpable; the liver was felt at the free margin of the ribs; the fingers were not clubbed; few retinal hemorrhages were present. The blood count showed: hemoglobin, 65 per cent; erythrocytes, 4,400,000; leukocytes, 34,000; polymorphonuclears, 88 per cent; lymphocytes, 12 per cent. The phenolsulphonphthalein test showed an excretion of 70 per cent in two hours. The urine showed a trace of albumin and a few erythrocytes and leukocytes. The blood showed: urea, 16.8 mg.; nonprotein nitrogen, 43.1; uric acid, 3.2; creatinine, 2.5; cholesterol, 0.296. The temperature ranged from 99 to 104 and was hectic in type.

Course of Illness.—On May 27, painful red spots were present on the pads of the toes and on the soles. The sternum was tender. On June 9, blood culture was positive for anhemolytic streptococci, showing 10 colonies per cubic centimeter. On June 4, the right lower quadrant of the abdomen was tender, and the right femoral pulse was not felt. Blood was not found in the stool. On June 10, edema of the right foot was present. On June 15, a palpable mass was felt in the right lower quadrant of the abdomen, which gave a thrill on palpation and a to and fro murmur on auscultation. The diagnosis was mycotic aneurysm. Dr. Emanuel Libman believed that the arteriovenous aneurysm was due to a patent ductus arteriosus or to a mycotic deposit on the wall of the pulmonary artery with perforation communicating with a pulmonary vein. Progressive dilatation of the superficial veins of the abdomen extended around toward the back over the crest of the ileum. A roentgenogram of the heart showed: enlargement to the left and right interpreted as being the picture of an advanced mitral lesion. The child died of a progressive anemia. Necropsy was not permitted.

CASE 6.—*History.*—A. W., a boy, aged 8 years, was admitted to the hospital on June 20, 1921, and died on July 12, 1921. He had had cardiac disease for the past three or four years and became tired easily but was never confined to bed.

Four weeks before admission, the child had begun to lose weight and had complained of occasional pains in the left side of the chest. The fingers and toes were painful, and pallor was progressive.

Physical Examination.—Clubbing of the fingers and toes, enlarged tonsils and presystolic, systolic and diastolic murmurs over the precordium were present; the spleen was not palpable but percussion showed that it extended down to the costal margin; petechiae were found with white centers over the left shoulder and on the conjunctivae; the liver was felt at the costal margin. The blood count showed: hemoglobin, 60 per cent; leukocytes, 9,000; polymorphonuclears, 65 per cent; lymphocytes, 31 per cent; monocytes, 4 per cent. The urine showed: no albumin and occasional erythrocytes and leukocytes. Blood culture was positive for anhemolytic streptococci, showing 100 colonies per cubic centimeter. A roentgenogram of the heart showed evidence of an advanced mitral and aortic lesion. The temperature ranged from 99 to 103 and was of the septic type.

Course of Illness.—On July 10, increased dyspnea and pallor were present; the liver was enlarged, and there was evidence of a terminal decompensation. The child died on July 12 as a result of the progressive decompensation which began only several days before death. Necropsy was not permitted.

CASE 7.—*History.*—G. N., a girl, aged 12½ years, was admitted to the hospital on Sept. 22, 1922, and died on Oct. 10, 1922.

The child had had nephritis at the age of 3 years and growing pains at the age of 3½ years; she also had had scarlet fever and diphtheria. During the past six years, the child had had arthritis and tonsillitis several times. She had been in apparently fairly good condition one month before admission, when she had become weak, had had chills and fever and slight dyspnea, and her face had become puffy.

Physical Examination.—A faint systolic murmur was present over the precordium; the spleen was large and hard and was felt five fingerbreadths below the costal margin; the liver was not palpable. The urine showed a trace of albumin and a moderate number of erythrocytes. A provisional diagnosis was made of malaria with nephritis, in view of the rigors and enlarged spleen. Gaucher's disease also was considered. The blood count showed: hemoglobin, 45 per cent; erythrocytes, 2,690,000; leukocytes, 4,200; polymorphonuclears, 61 per cent; lymphocytes, 36 per cent; monocytes, 1 per cent; myelocytes, 2 per cent. The blood pressure on admission was 184 systolic; 122, diastolic. On September 26, petechiae were present in the conjunctivae, and the fingers were slightly clubbed. Blood cultures on September 26 and October 3 were negative. The urine showed: specific gravity, from 1.006 to 1.012; albumin, +; erythrocytes and leukocytes. Blood chemical determinations showed: urea nitrogen, 16.8 mg.; nonprotein nitrogen, 49; uric acid, 2.7; creatinine, 1.3; cholesterol, 0.208.

Course of Illness.—The patient was afebrile for several weeks after admission. She left the hospital against advice, but was readmitted after being home only a few days. She again had chills and had sharp pain in the left hypochondrium and right leg. She vomited blood. On October 6, the systolic murmur increased in intensity and was loudest at the base. On October 7, Dr. Emanuel Libman thought that the child had a mycotic aneurysm in view of the character of the murmur which was also heard posteriorly in the interscapular region, although such a murmur may be heard in persons with congenital stenosis of the isthmus of the aorta. On October 8, the hemoglobin was 25 per cent. The child died of progressive anemia.

Necropsy.—Congenital stenosis of the isthmus of the aorta, multiple infarctions of the spleen, mycotic endarteritis and saccular aneurysm of the descending portion of the thoracic aorta were found. On the mitral valve were pinkish gray vegetations harboring numerous bacteria which on culture proved to be anhemolytic streptococci. These organisms were also isolated from the aneurysm. The kidneys showed a subacute diffuse glomerular involvement. They were tan-gray and presented the picture of so-called "flea-bitten" kidney.

CASE 8.—*History.*—M. S., a girl, aged 8 years, was admitted to the hospital on Sept. 20, 1922, and died on Feb. 9, 1923. The child had not had rheumatism, chorea or tonsillitis, as far as could be determined. For the past three years it had been known that she had heart trouble. Tonsillectomy had been performed two years before admission to the hospital. She had been up and about as usual until five weeks before admission, when she had begun to have fever, had felt weak and had had ten teeth extracted, without improvement in her general condition.

Physical Examination.—Presystolic and systolic murmurs over the cardiac apex, numerous petechiae over the chest, arms and body and a palpable spleen were present. The blood count showed: hemoglobin, 76 per cent; leukocytes, 10,300; polymorphonuclears, 76 per cent; eosinophils, 2 per cent; lymphocytes, 22 per cent; no histiocytes. The Wassermann reaction was negative. The blood pressure was 112 systolic; 76, diastolic.

Course of Illness.—On September 23, petechiae were found in both lower conjunctivae. The temperature ranged from 99 to 103, some fever being present nearly every day. The urine showed: specific gravity, 1.010 and 1.020, a trace of albumin and a few erythrocytes and leukocytes and hyaline casts. Petechiae, some white centered, appeared daily. The child was apparently in good condition and happy. On November 19, about two months after admission, a beginning café au lait color of the skin was noted. The phenolsulphonphthalein test on September 20, showed a return of 70 per cent in two hours; on December 24, it showed 28 per cent in two hours and hemoglobin, 47 per cent, and erythrocytes, 3,700,000. On December 28, numerous retinal hemorrhages occurred. On January 5, sharp abdominal pain and vomiting occurred. The spleen was tender to palpation. The diagnosis was splenic infarct. On February 9, headache, facial palsy and positive Kernig and Brudzinski signs were present, and the tongue deviated to the left. The neurologic signs progressed, and the child went into coma and died. Blood cultures taken five times during her stay in the hospital showed a growth of from 120 to 500 colonies per cubic centimeter of anhemolytic streptococci. Repeated blood chemical studies showed: urea from 12 to 16 mg.; nonprotein nitrogen, from 35 to 42 and creatinine, from 1 to 1.5 and uric acid, from 1.5 to 2. The cholesterol was 0.118. A roentgenogram of the heart showed it to have a mitral configuration. Necropsy was not performed, but the case was definitely one of subacute bacterial endocarditis, with a typical condition found on blood culture. Intravenous injection of sodium cacodylate was used repeatedly, without effect on the presence of bacteria in the blood.

CASE 9.—*History.*—H. K., a boy, aged 6 years, was admitted to the hospital on Aug. 25, 1924. He was taken home against advice in a dying condition on Nov. 21, 1924.

He had had repeated attacks of rheumatic fever in the past. About six weeks before admission, he again had had pains in the joints. A valvular lesion had been present at that time. Three weeks before admission he had begun to have headaches, had become weak, lost weight and continued to have pains in the joints.

Physical Examination.—Clubbed fingers, a presystolic murmur and white centered petechiae were present; the spleen was palpable two fingerbreadths below the costal margin; the knees were slightly tender but were not swollen or reddened. Subcutaneous nodules were not present. The blood count showed: leukocytes, 10,000; polymorphonuclears, 80 per cent; lymphocytes, 20 per cent; erythrocytes, 4,000,000; hemoglobin, 65 per cent. On August 29, severe headache, sharp pain in the left hypochondriac region and vomiting occurred. White centered petechiae appeared and disappeared daily. Blood cultures showed: anhemolytic streptococci in dextrose broth. Because of the difficulty in obtaining sufficient blood, plates could not be made. The urine showed a trace of albumin with erythrocytes and leukocytes. The temperature ranged from 99 to 103 and was hectic in type.

Course of Illness.—The patient left the hospital against advice; so the termination of the case is not known. This case had all the clinical features with the blood culture manifestations of a case of subacute bacterial endocarditis.

Case 10.—*History.*—J. H., a girl, aged 12½ years, was admitted to the hospital on April 7, 1925, and died on June 12, 1925. Tonsillectomy had been performed when the patient was 4 years old. It is not known whether she had had rheumatic fever. She had had an indefinite cardiac history for the past four years and occasional cardiac palpitation on exertion during the past three years. Three months before admission, she had begun to have pains in the legs. Moments of dizziness, which she had had for three weeks, was the cause of her admission to the hospital.

Physical Examination.—Slight pallor, a slightly enlarged heart and a presystolic, systolic and diastolic murmurs were present; the spleen and liver were palpable at the costal margin. On admission the blood count showed: hemoglobin, 85 per cent; leukocytes, 6,000; polymorphonuclears, 76 per cent; lymphocytes, 24 per cent. The blood pressure was 100 systolic; 45, diastolic.

Course of Illness.—On April 10, cramplike abdominal pain was present. On April 12, a bloody stool was passed. The temperature was continually irregular, the temperature ranging from 100 to 104 F. Blood cultures on April 15 and April 23 were positive for anhemolytic streptococci. Petechiae were not noted on admission, but they appeared from time to time shortly thereafter. On April 21, a presystolic thrill was present; the anemia was progressive, and the hemoglobin was falling gradually to 35 per cent. Chemical determination of the blood on May 2 showed: urea, 14; nonprotein nitrogen, 34.1; uric acid, 2.5; creatinine, 1. The urine showed a trace of albumin, hyaline casts and occasional erythrocytes. On May 7, beginning clubbing of the fingers was noticed. On May 26, the blood count showed: leukocytes, 8,000; polymorphonuclears, 82 per cent; lymphocytes, 18 per cent. On May 27, pain was felt in the right hyperchondrium, and the patient expectorated bloody sputum. Roentgen-ray examination made when the patient was admitted to the hospital showed that the chest was normal, but such an examination now showed a shadow at the base of the right lung which in view of the hemoptysis, was probably due to infarction. The spleen and liver had progressively become enlarged and were tender. On May 28, a tender, swollen, erythematous area was present on the dorsum of the right foot. On June 10, the patient vomited frequently and was edematous. The urine showed: albumin, + + and many hyaline casts and erythrocytes. She died in decompensation.

Necropsy.—Numerous greenish, large and small, friable vegetations, especially along the edge of the mitral valve and also on the chordae tendinae and on the posterior wall of the left ventricle, were found. Some of these vegetations were

also found on the aortic valve. They were typical of those found in subacute bacterial endocarditis. Aschoff bodies were not found in the myocardium. The spleen, liver and lung showed infarcts, and the kidneys showed a typical focal embolic glomerular nephritis. Terminal bronchopneumonia and a subacute encephalitis also were present.

CASE 11.—*History.*—M. H., a girl, aged 10 years, was admitted to the hospital on July 26, 1926, and died on Aug. 2, 1926. Five years before admission, she had had scarlet fever complicated by arthritis. Her cardiac history is said to have dated from within a year of the scarlet fever. She had had frequent attacks of tonsillitis, and her tonsils had been removed three years before admission. She had attended a cardiac clinic and had been told that she had a murmur. She attended school regularly, had a good appetite and developed normally. Two weeks before admission to the hospital, she began to have fever and pain in the knees.

Physical Examination.—Nutrition was good; the child was cheerful, and decompensation was not present; the temperature was 103 F.; the heart was slightly enlarged with a blowing systolic murmur at the apex; the spleen was hard and descended well below the free border of the ribs; suspicious petechiae were present below the left clavicle. The blood count showed: hemoglobin, 65 per cent; erythrocytes, 3,870,000; leukocytes, 13,200; polymorphonuclears, 72 per cent; lymphocytes, 28 per cent. Histiocytes were not seen. Blood culture was positive for anhemolytic streptococci; the colonies were too numerous to count. The temperature was irregular, from 99 to 103 F. The urine did not show any albumin and a few erythrocytes and leukocytes.

Course of Illness.—On August 1, headache and vomiting were present; the temperature rose to 104 F.; the child cried out and soon became unconscious. She developed the typical signs of cerebral embolus and died within twenty-four hours, with hyperpyrexia. Before her death she developed many more petechiae.

Necropsy.—The heart showed an irregular thickening of the mitral valve. At the midpoint on the anterior surface of one flap, there was an irregular tab which was characteristic of a typical bacterial vegetation. The kidney was congested. The spleen showed an irregular surface but no infarction, and infarction of any other organ was not present. Permission for the removal of the brain was not obtained, but there is little doubt clinically that death resulted from a cerebral embolus. This was a case of early yet definite bacterial endocarditis with a single vegetation.

CASE 12.—*History.*—J. S., a boy, aged 11 years, was first admitted to the hospital on Feb. 27, 1927, and was discharged on April 16, 1927. He had had measles when he was 6 years old, but no history of rheumatic fever. In September, 1925, or about one and one-half years before entering the hospital, the child had had sore throat and a temperature of 102 F. and the mother had observed that the child's heart was visibly pulsating against the wall of the chest. After two weeks in bed, he had returned to school. He did not have any complaints at that time, except a slight shortness of the breath on climbing stairs or on vigorous exercise and an occasional slight hacking cough. In May, 1926, tonsillectomy had been performed. In December, 1926, he had become ill again and had had a temperature of 103 F. and pallor, pain in the ankles and profuse sweats. He had been more or less constantly in bed since that time. During the latter part of January, 1927, he had developed fever and swollen, tender wrists and had been admitted to the hospital.

Physical Examination.—Pallor, slight cyanosis, clubbing of the fingers and toes and numerous petechiae, some of which had white centers were present both on the lower conjunctivae and over the volar aspect of the forearms; the heart was

somewhat enlarged with a presystolic and systolic murmur at the apex and a diastolic murmur at the base transmitted downward; slight decompensation was present; the spleen was palpable, quite hard and descended well below the costal margin with respiration; the right ankle was slightly swollen and tender; the heart rate was 120; the temperature on admission was 103 F. The fundi were normal. The provisional diagnosis was subacute bacterial endocarditis.

A roentgenogram of the heart showed a hypertrophied and dilated left ventricle and also a right sided enlargement. Blood culture on admission and one taken on March 13 were both negative both aerobically and anaerobically. Freshly voided specimens of urine on fifteen different occasions did not contain albumin and erythrocytes. The phenolsulphonphthalein test showed an excretion of 60 per cent in two hours. The blood Wassermann test was negative.

Course of Illness.—The temperature ranged irregularly up to 103, but the child was afebrile for weeks. The diastolic murmur heard on admission developed a musical quality.

On March 17, the patient noted that his fingers and toes were tender. On March 19, he vomited and had sharp pain in the left upper abdominal quadrant, which was interpreted as a possible splenic infarct. On March 21, he vomited repeatedly, and sharp pain was present in the left upper abdominal quadrant; probably there was a second splenic infarct, and the systolic and diastolic murmurs were more musical. On March 27, several tender purplish red areas, about 3 mm. in diameter were noticed on both soles. On April 9, the spleen was definitely smaller, perhaps harder than previously probably following infarctions. On March 26, the blood pressure was 105 systolic; 55, diastolic. On April 13, it was 102 systolic; 62, diastolic. New petechiae were not seen for one month between March 13 and April 11. On April 13, petechiae were again seen in the conjunctivae and below the clavicles. On March 5, blood chemical studies showed: urea, 17; uric acid, 3. On March 1, the blood count showed: hemoglobin, 67 per cent; erythrocytes, 4,000,000; leukocytes, 13,200; polymorphonuclears, 52 per cent; lymphocytes, 48 per cent. On April 13, the hemoglobin was 55 per cent. On April 16, the patient was referred to the cardiac outpatient department.

Readmission.—The child was readmitted on Oct. 19, 1927. He had been in bed at varying intervals during the past six months. He had been placed in bed only when it was noted that he had fever; otherwise, he had played about the streets as usual and had not had any discomfort. A blood culture taken during July from the outpatient department had been negative. A few days before readmission, the child had begun to have severe headaches, and he felt weak and vomited. The day of admission he had had a severe nose bleed. His temperature had also been from 102 to 103 for several days before he was admitted.

The temperature on admission was 104 F.; the pulse rate, 140; the boy had moderate dyspnea and was perspiring profusely; the skin had a distinct café au lait color, which had been absent on the previous admission. The heart murmurs were much louder than before; the heart was enlarged to a greater extent than previously; there was much more thrust to the precordium with each beat; clubbing was more marked; the spleen was hard and readily palpable; petechiae were present over the left side of the neck and over the shoulder; the patient showed a marked capillary pulse. Blood cultures taken on October 19, October 24, and October 26, were negative aerobically and anaerobically. The blood pressure was 118 systolic; 70, diastolic. On October 24, left facial paresis occurred and the tongue deviated slightly to the left; signs of meningitis were not present. The fundi were normal. October 25 a few tender, slightly raised red areas appeared on the toes. On October 26, severe headache, vomiting and sharp pain

in the left upper quadrant occurred. The blood count showed on admission: hemoglobin, 55 per cent; erythrocytes, 2,680,000; leukocytes, 7,400; polymorphonuclears, 70 per cent; lymphocytes, 30 per cent. The urine showed a faint trace of albumin and an occasional leukocyte but no erythrocytes. On October 27, the patient died suddenly during the night. The facial paralysis remained. It was probable that he died from a cerebral embolus, as there were no other signs preceding his death.

Necropsy was not permitted. In view of the negative bacteriologic studies, this case was probably one of subacute bacterial endocarditis in the bacteria-free stage.

SUMMARY

Attention is called to the fact that subacute bacterial endocarditis in childhood is not rare, although one may be led to believe this because some of the best textbooks on pediatrics fail to mention this disease. The literature has been reviewed and reports of sixty-four cases in children under 14 years of age have been collected.[27] We have reported twelve additional cases in children under 13 years of age.

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27. Since this paper was finished, it has come to our attention that J. D. Nourse reported four cases of subacute bacterial endocarditis in children, aged 10 years or younger, at the meeting of the Central States Pediatric Society, Cleveland, Oct. 14, 1927.

METABOLISM OF UNDERNOURISHED CHILDREN

VII. EFFECT OF HIGH AND LOW PROTEIN DIETS ON THE NITROGEN AND CALORIC BALANCE OF UNDERNOURISHED CHILDREN *

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The following investigation was undertaken for the purpose of determining the possible relationship between the nitrogen intake and the rate of growth in normal and undernourished children. Two series of experiments were therefore performed on eight normal and nine undernourished children of from 4 to 12 years of age, using in the first series a high protein, and in the second a low protein diet.[1] Nineteen experiments, of at least seven days' duration each, were performed in each series, the children being divided into three groups as follows: group 1, the vigorous normal children; group 2, children from 0.0 to 9.9 per cent underweight, and group 3, children 10 per cent or more underweight for their height and age.

The same technic of feeding, collection of specimens and chemical analysis of food and excreta was observed in these experiments as has already been described in previous papers of this series.[2] The diets were planned to contain an equal number of calories, with 2 Gm. of protein per kilogram of body weight for the low diet, and 4 Gm. of protein per kilogram for the high. In actual practice, however, considerable

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1. The so-called low protein diet was low only in comparison with the other diets used in this series of investigations, and actually contained 10 per cent of its calories in the form of protein, an amount of protein which would be considered adequate according to the figures given by Rose (Laboratory Manual for Dietetics, revised ed., New York, 1925).

2. Wang, C. C.; Frank, M.; Kern, R., and Hays, B. B.: Metabolism of Undernourished Children: III. Urinary Nitrogen with Special Reference to Creatinine, Am. J. Dis. Child. **32**:360 (Sept.) 1926. Wang, C. C.; Witt, D. B., and Felsher, A. B.: A Comparison of the Metabolism of Some Mineral Constituents of Cow's Milk and of Breast Milk in the Same Infant, Am. J. Dis. Child. **27**:352 (April) 1924. Wang, C. C.; Kaucher, M., and Frank, M.: Metabolism of Undernourished Children: VI. Calory Balance **35**:856 (May) 1928.

variation was found to occur in both the caloric intake and the nitrogen intake, the calories varying from 76.3 to 122.4 per kilogram of body weight, and the nitrogen varying from 0.436 to 0.682 Gm. per kilogram on the high protein diet. On the low protein diet, the caloric range was from 51.1 to 97.2 calories per kilogram and the nitrogen range from 0.201 to 0.404 Gm. per kilogram. This variation was due partly to the discrepancy between the published figures and the actual nitrogen content of the foods as analyzed, and partly to the fact that some of the children refused to eat the amount planned.

A typical day's diet for a girl, aged 8 years, weighing 20.7 Kg. on the high protein level is as follows: milk, 1,000 Gm.; eggs, 50 Gm.; meat, 120 Gm.; orange juice, 500 Gm.; tomato, 300 Gm.; potato, 150 Gm.; farina, 125 Gm.; bread, 30 Gm.; butter, 3 Gm.; sugar, 16 Gm. On the low protein diet, the same child ate 600 Gm. of milk, 38 Gm. of egg, 400 Gm. orange juice, 200 Gm. tomato, 200 Gm. potato, 48 Gm. sugar, 52 Gm. butter, the same quantities of bread and farina, and no meat. It will be seen that the low diet still contains a high proportion of a good quality of animal protein, what is generally considered to be an adequate amount of milk, and an abundance of vitamins A, B and C. We believe, therefore, that any differences in gain in weight which may have occurred in the children on the two diets are actually due to the differences in the quantity of protein consumed and not to differences in quality of protein or quantity of vitamins.

COMMENT

In tables 1 and 2 are given the data concerning the caloric balance in children fed on the high and low protein diets. It will be seen that on both diets the percentage utilization fell within the range reported in our previous investigation [3] on the caloric balance, and may be considered normal for both groups on both diets. The utilization, however, was slightly higher on the low protein than the high protein diet.

The caloric loss in all groups, in both urine and feces, was higher on the high protein diet than on the low. This is probably accounted for by three possible factors, namely, the increased caloric value of the urine due to the higher content of nitrogenous substances such as urea, uric acid etc., on the high protein diet; the increased caloric value of the feces due to a larger amount of indigestible connective tissue on the high protein diet, and finally, the fact that the average caloric intake was higher in all groups on the high protein diet than on the low. This supports the conclusion drawn in our former paper [3] that the total caloric loss is entirely dependent on the total caloric intake.

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3. Wang; Kaucher and Frank (footnote 2, third reference).

TABLE 1.—*Influence of High Protein Diet on Caloric Balance*

Name	Sex	Age	Weight		Caloric Intake		Caloric Output per 24 Hrs.						Utilization			Ratio of Calories to Nitrogen	Variation in Weight per 24 Hrs. Gm.
							Urine		Feces		Total						
			Kilo	Variation from Normal Per Cent	24 Hrs. Gm.	Per Kg. of Body Weight Gm.	Total Gm.	Per Kg. of Body Weight Gm.	Total Gm.	Per Kg. of Body Weight Gm.	24 Hrs. Gm.	Per Kg. of Body Weight Gm.	Total Gm.	Per Kg. of Body Weight Gm.	Percent of Intake		
Vigorous Normal																	
R. W.	F	11	35.4	+ 8.3	2,754	78.0	88	2.5	145	4.1	233	6.6	2,521	71.2	91.5	7.7	+100
S. W.	F	8	21.9	+ 1.4	2,524	115.2	69	3.2	133	6.0	202	9.2	2,322	106.0	92.0	7.4	+ 71
A. Ge.	F	5	17.9	+ 0.6	2,192	122.4	48	2.7	80	4.4	128	7.1	2,064	115.3	94.2	6.1	+129
J. G.	M	8	23.8	+ 0.0	2,357	99.0	67	2.8	104	4.4	171	7.2	2,186	91.8	92.8	7.7	+ 71
B. L.	F	11	31.3	— 1.6	2,436	77.8	86	2.7	102	3.3	188	6.0	2,248	71.8	92.3	7.3	+ 43
F. J.	F	10	27.5	— 2.5	2,441	88.8	83	3.0	108	3.9	191	6.9	2,250	81.8	92.2	7.2	+ 43
R. G.	F	10	27.9	— 3.1	2,413	86.5	43	1.5	117	4.2	160	5.7	2,253	80.8	93.4	3.9	+ 71
K. B.	F	8	20.7	— 3.7	1,655	80.0	69	3.3	96	4.6	165	8.0	1,490	72.0	90.0	6.9	+ 71
Average		8.9	25.8	— 0.1	2,347	93.4	69	2.7	111	4.4	180	7.1	2,167	86.3	92.3	6.8	+ 75
From 0.0 to 9.9 Per Cent Underweight																	
W. K.	M	12	28.6	— 5.3	2,052	76.3	83	2.9	87	3.0	170	5.9	1,882	65.8	91.7	5.9	+100
G. C.	M	10	26.9	— 5.3	2,249	78.6	84	3.1	109	4.1	193	7.2	2,056	76.4	91.4	5.9	+ 71
A. G	F	10	27.6	— 6.1	2,500	90.6	90	3.3	145	5.2	235	8.5	2,265	82.1	90.6	7.3	+ 71
H. K.	M	10	21.7	— 8.8	1,737	80.0	83	3.8	78	3.6	161	7.4	1,576	72.6	90.7	7.7	+ 86
Average		10.5	26.2	— 6.4	2,135	81.4	85	3.3	105	4.0	190	7.3	1,945	74.2	91.1	6.7	+ 82
Over 10 Per Cent Underweight																	
K. Bo.	F	8	20.6	—10.5	1,655	80.3	81	3.9	102	5.0	183	8.9	1,472	71.5	89.0	8.4	+ 71
E. S.	F	4	13.7	—11.0	1,046	76.3	51	3.7	36	2.6	87	6.3	959	70.0	91.7	7.0	+114
F. B.	F	10	17.8	—13.2	1,447	81.3	77	4.3	73	4.1	150	8.4	1,297	72.9	89.7	8.3	+ 43
L. B.	F	11	25.8	—17.8	2,089	81.0	101	3.9	115	4.5	216	8.4	1,873	72.6	89.7	9.0	+100
A. B.	F	6	16.9	—18.0	1,799	106.5	50	3.0	81	4.8	131	7.8	1,668	98.7	92.7	7.3	+ 86
A. G.	F	10	22.7	—21.2	2,226	98.0	78	3.4	199	8.8	277	12.2	1,949	85.9	87.6	7.5	+114
A. G.	F	10	20.6	—27.0	2,202	101.9	66	3.2	155	7.5	221	10.7	1,981	96.2	90.0	7.8	+114
Average		8.4	19.7	—17.0	1,781	90.0	72	3.6	109	5.3	181	9.0	1,600	81.1	90.1	7.9	+ 92

TABLE 2.—*Influence of Low Protein Diet on Caloric Balance*

Name	Sex	Age	Weight		Caloric Intake		Caloric Output per 24 Hrs.						Utilization			Ratio of Calories to Nitrogen	Variation in Weight per 24 Hrs. Gm.
							Urine		Feces		Total						
			Kilo	Variation from Normal Per Cent	24 Hrs. Gm.	Per Kg. of Body Weight Gm.	Total Gm.	Per Kg. of Body Weight Gm.	Total Gm.	Per Kg. of Body Weight Gm.	24 Hrs. Gm.	Per Kg. of Body Weight Gm.	Total Gm.	Per Kg. of Body Weight Gm.	Percent of Intake		
Vigorous Normal																	
R. W.	F	11	34.7	+ 6.1	1,775	51.1	57	1.7	96	2.8	153	4.5	1,622	46.7	91.4	8.7	— 43
H. P.	F	4	16.5	— 1.2	1,233	74.7	34	2.1	53	3.2	87	5.3	1,146	69.4	92.9	7.7	— 29
B. L.	F	11	30.9	— 2.8	1,784	57.7	50	1.6	78	2.5	128	4.2	1,656	53.6	92.8	8.5	— 71
S. W.	F	8	21.0	— 2.8	1,652	78.7	43	2.1	72	3.4	115	5.5	1,537	73.2	93.1	8.3	— 43
A. Ge.	F	5	17.1	— 3.9	1,661	97.2	32	1.9	80	4.7	112	6.6	1,549	90.6	93.2	7.4	± 00
F. J.	F	10	26.9	— 4.6	1,781	66.2	46	1.7	86	3.2	132	4.9	1,649	61.3	92.6	8.4	± 00
K. B.	F	8	20.5	— 4.7	1,616	80.3	47	2.3	59	2.9	106	5.2	1,540	75.1	93.5	9.0	+ 14
Average		8.1	22.9	— 2.0	1,655	72.3	44	1.9	75	3.2	119	5.2	1,528	67.1	92.8	8.3	— 25
From 0.0 to 9.9 Per Cent Underweight																	
W. K.	M	12	28.5	— 5.6	2,248	78.9	51	1.8	69	2.4	120	4.2	2,128	74.7	94.7	7.6	+ 57
R. G.	F	10	27.1	— 5.9	1,777	65.6	47	1.8	77	2.8	124	4.6	1,653	61.0	93.0	8.9	+ 14
A. G.	F	10	27.5	— 6.5	1,775	64.5	47	1.7	110	4.0	157	5.7	1,618	58.8	91.2	8.3	+ 14
G. C.	M	10	26.0	— 7.5	2,371	91.2	54	2.1	35	1.3	88	3.4	2,283	87.8	96.3	7.0	+ 43
H. K.	M	10	21.6	— 9.3	1,725	79.9	50	2.3	56	2.6	86	4.0	1,639	75.9	95.0	8.4	+ 14
Average		10.2	26.1	— 6.9	1,979	76.0	50	1.9	69	2.6	115	4.4	1,864	71.6	94.0	8.0	+ 28
Over 10 Per Cent Underweight																	
A. B.	F	6	18.6	—11.0	1,334	71.7	37	2.0	63	3.4	100	5.4	1,223	65.8	92.4	9.3	+ 14
K. Bo.	F	8	20.2	—12.2	1,650	81.7	58	2.9	44	2.1	102	5.0	1,548	76.6	93.4	12.8	+ 29
F. B.	F	10	17.5	—14.7	1,434	81.9	52	3.0	62	3.5	114	6.5	1,320	75.4	92.0	11.4	± 00
E. S.	F	4	12.7	—15.9	1,168	92.0	33	2.6	29	2.4	62	5.0	1,106	87.1	94.7	8.2	+ 29
M. D.	F	7	18.5	—16.3	1,421	76.8	38	2.1	69	3.7	107	5.8	1,314	71.0	92.5	7.3	+ 14
L. B.	F	11	25.1	—20.1	2,034	81.0	73	2.9	59	2.3	132	5.2	1,902	75.8	93.5	13.1	+ 43
A. B.	F	6	16.4	—20.4	1,394	85.0	28	1.7	80	4.7	108	6.6	1,286	78.4	92.2	8.7	+ 71
A. G.	F	10	22.2	—22.9	1,431	64.4	48	2.1	112	5.1	160	7.2	1,271	57.3	88.8	10.6	± 00
A. G.	F	10	20.1	—28.7	1,439	71.6	34	1.7	103	5.1	138	6.8	1,301	64.7	90.5	8.1	+ 43
Average		8	19.0	—18.0	1,478	78.5	45	2.3	69	3.6	114	5.9	1,363	72.5	92.2	9.9	+ 27

The ratio of calories to nitrogen falls within the normal range according to Utheim [4] in all groups on both diets, although the ratio is found to be considerably higher in the three groups on the low diet. As the total caloric loss depends on the caloric intake, and the nitrogen loss also depends on the protein intake, when two diets are equal in caloric value, the ratio of calories to nitrogen in the urine will, of course, be found to be in inverse proportion to the intake.

In tables 3 and 4 are given the data concerning the nitrogen metabolism in the groups of children on the same high and low protein diets. On the high protein diet, it was found that the percentage retention was about the same for both groups of normal and undernourished children. On the other hand, on the low protein diet the percentage retention was much higher for the undernourished children than for the normal children, the latter actually showing a negative balance in a majority of cases. This is probably due to the fact that the normal children were accustomed to a diet higher in protein, and were not yet adjusted to a lower protein level, and also because the nitrogen content of their bodies was relatively high, while the undernourished children had been undergoing a period of protein starvation and the nitrogen content of their bodies was low. Rubner, quoted by Lusk,[5] states that in the animal body the retention of protein depends on the protein content of the animal as well as on the quantity of protein ingested, and that of the same diet of protein more will be retained when the nitrogen content of the animal (dog) is low than when it is high. He also states that a small protein intake may cause the same retention of nitrogen as a large protein intake, if in the first instance there be a relative impoverishment of the protein content of the animal.

The nitrogen storage per kilogram of body weight was twice as high for the groups of undernourished children on the high protein as on the low protein diet, the nitrogen intake also being about twice as high on the former diet.

A comparison of the gains in weight in grams per twenty-four hours shows a striking difference in the average gain in all groups on the two diets. In all three groups the gain was much greater on the high protein diet than on the low. On the high protein diet, the undernourished children gained a little more rapidly than the normal, although all groups were making satisfactory gains. On the low protein diet, however, only one of the seven normal children made any gain. Three of these children actually lost weight, and three remained stationary.

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4. Utheim, K.: Metabolism Studies in Infants Suffering from Chronic Nutritional Disturbances (Athrepsia), Am. J. Dis. Child. **22**:329 (Oct.) 1921.

5. Rubner, quoted by Lusk, G.: The Science of Nutrition, ed. 3, Philadelphia, W. B. Saunders Company, 1921, p. 287.

TABLE 3.—*Influence of High Protein Diet on Nitrogen Balance*

Name	Sex	Age	Weight		N Intake		N Output per 24 Hours						Absorption per 24 Hrs.			Retention per 24 Hrs.			
							Urine		Feces		Total								
			Kilo	Variation from Normal Per Cent	24 Hrs. Gm.	Per Kg. of of Body Weight Gm.	Total Gm.	Per Kg. of of Body Weight Gm.	Total Gm.	Per Kg. of Body Weight Gm.	24 Hrs. Gm.	Per Kg. of Body Weight Gm.	Total Gm.	Per Kg. of Body Weight Gm.	Per Cent of Intake	Total Gm.	Per Kg. of Body Weight Gm.	Per Cent of Intake	Variation in Weight Gm.
Vigorous Normal																			
R. W.	F	11	35.4	+ 8.3	1,544	0.436	11.45	0.323	1.97	0.056	13.42	0.379	13.47	0.381	87.2	2.02	0.057	13.1	+100
S. W.	F	8	21.9	+ 1.4	13.90	0.635	9.35	0.427	1.46	0.067	10.81	0.494	12.44	0.568	89.5	3.09	0.141	22.2	+ 71
A. Ge.	F	5	17.9	+ 0.6	12.20	0.682	7.90	0.441	1.22	0.068	9.12	0.509	10.98	0.613	90.0	3.08	0.172	25.2	+129
J. G.	M	8	23.8	± 0.0	12.43	0.522	8.70	0.366	1.12	0.047	9.82	0.413	11.32	0.476	91.0	2.62	0.110	21.7	+ 71
B. L.	F	11	31.3	— 1.6	13.80	0.441	11.85	0.379	1.48	0.047	13.33	0.426	12.32	0.394	89.3	0.47	0.015	3.4	+ 43
F. J.	F	10	27.5	— 2.5	13.86	0.504	11.50	0.418	1.58	0.057	13.08	0.476	12.28	0.447	88.6	0.78	0.028	5.6	+ 43
R. G.	F	10	27.9	— 3.1	13.74	0.492	10.90	0.391	1.72	0.062	12.62	0.452	12.02	0.431	87.5	1.12	0.040	8.2	+ 71
K. B.	F	8	20.7	— 3.7	12.13	0.586	10.02	0.484	1.13	0.055	11.15	0.539	11.00	0.531	90.7	0.98	0.047	8.1	+ 71
Average		8.9	25.8	— 0.1	13.44	0.537	10.21	0.403	1.46	0.057	11.67	0.461	11.98	0.480	89.2	1.77	0.076	13.4	+ 75
From 0.0 to 9.9 Per Cent Underweight																			
W. K.	M	12	28.6	— 5.3	18.07	0.632	14.15	0.495	1.54	0.054	15.69	0.549	16.53	0.578	91.5	2.38	0.083	13.2	+100
G. C.	M	10	26.9	— 5.3	17.79	0.661	14.17	0.527	1.19	0.044	15.36	0.571	16.60	0.617	93.3	2.43	0.090	13.7	+ 71
A. G.	F	10	27.6	— 6.1	13.95	0.505	12.25	0.444	1.33	0.048	13.58	0.492	12.62	0.457	90.5	0.37	0.013	2.7	+ 71
H. K.	M	10	21.7	— 8.8	13.73	0.633	10.74	0.495	0.80	0.037	11.54	0.532	12.93	0.596	94.2	2.19	0.101	16.0	+ 86
Average		10.5	26.2	— 6.4	15.89	0.608	12.83	0.490	1.22	0.046	14.04	0.536	14.67	0.562	92.4	1.84	0.072	11.4	+ 82
Over 10 Per Cent Underweight																			
K. Bo.	F	8	20.6	—10.5	13.27	0.644	9.69	0.470	1.40	0.068	11.09	0.538	11.87	0.576	89.5	2.18	0.106	16.4	+ 71
E. S.	F	4	13.7	—11.0	9.13	0.666	7.29	0.532	0.48	0.035	7.77	0.567	8.65	0.631	94.7	1.37	0.100	15.0	+114
F. B.	F	10	17.8	—13.2	10.38	0.583	9.30	0.522	0.87	0.049	10.17	0.571	9.51	0.534	91.6	0.21	0.012	2.0	+ 43
L. B.	F	11	25.8	—17.8	16.31	0.632	11.25	0.436	1.62	0.063	12.87	0.499	14.69	0.569	90.1	3.44	0.133	21.1	+100
A. B.	F	6	16.9	—18.0	9.58	0.567	6.84	0.405	1.41	0.083	8.25	0.488	8.17	0.483	85.3	1.33	0.079	13.9	+ 86
A. G.	F	10	22.7	—21.2	13.97	0.615	10.36	0.456	1.59	0.070	11.95	0.526	12.38	0.545	88.6	2.02	0.089	14.5	+114
A. G.	F	10	20.6	—27.0	13.71	0.666	8.42	0.409	1.62	0.079	10.04	0.487	12.09	0.587	88.2	3.67	0.178	25.8	+114
Average		8.4	19.7	—17.0	12.34	0.625	9.02	0.461	1.28	0.064	10.31	0.525	11.05	0.561	89.7	2.03	0.100	15.7	+ 92

TABLE 4.—*Influence of Low Protein Diet on Nitrogen Balance*

Name	Sex	Age	Weight		N Intake		N Output per 24 Hours						Absorption per 24 Hrs.			Retention per 24 Hrs.			
							Urine		Feces		Total								
			Kilo	Variation from Normal Per Cent	24 Hrs. Gm.	Per Kg. of of Body Weight Gm.	Total Gm.	Per Kg. of of Body Weight Gm.	Total Gm.	Per Kg. of Body Weight Gm.	24 Hrs. Gm.	Per Kg. of Body Weight Gm.	Total Gm.	Per Kg. of Body Weight Gm.	Per Cent of Intake	Total Gm.	Per Kg. of Body Weight Gm.	Per Cent of Intake	Variation in Weight Gm.
Vigorous Normal																			
F. W.	F	11	34.7	+ 6.1	7.04	0.203	6.55	0.189	1.23	0.035	7.78	0.224	5.81	0.167	82.5	—0.74	—0.021	—10.5	— 43
J. G.	M	8	23.5	— 1.3	5.72	0.243	4.90	0.209	0.90	0.038	5.80	0.247	4.82	0.205	84.2	—0.08	—0.003	— 1.4	± 00
B. L.	F	11	30.9	— 2.8	6.22	0.201	5.90	0.191	1.03	0.033	6.93	0.224	5.19	0.168	83.4	—0.71	—0.023	—11.4	— 71
S. W.	F	8	21.0	— 2.8	6.41	0.305	5.15	0.245	0.89	0.042	6.04	0.288	5.52	0.263	86.1	0.37	0.018	5.8	— 43
A. Ge.	F	5	17.1	— 3.9	5.86	0.343	4.35	0.254	1.07	0.063	5.42	0.317	4.79	0.280	81.7	0.44	0.026	7.5	± 00
F. J.	F	10	26.9	— 4.6	6.66	0.248	5.50	0.204	1.37	0.051	6.87	0.255	5.29	0.197	79.4	—0.21	—0.008	— 3.1	± 00
K. B.	F	8	20.5	— 4.7	6.32	0.308	5.23	0.255	0.72	0.035	5.95	0.290	5.60	0.273	88.6	0.37	0.018	5.9	+ 14
Average		8.9	24.9	— 2.0	6.32	0.264	5.37	0.221	1.03	0.042	6.39	0.264	5.29	0.222	83.7	—0.08	0.001	0.4	— 20
From 0.0 to 9.9 Per Cent Underweight																			
W. K.	M	12	28.5	— 5.6	9.89	0.347	6.75	0.237	0.98	0.034	7.73	0.271	8.91	0.313	90.1	2.16	0.076	21.8	+ 57
R. G.	F	10	27.1	— 5.9	6.61	0.244	5.30	0.196	1.12	0.041	6.25	0.231	5.49	0.203	83.1	0.36	0.013	5.4	+ 14
A. G.	F	10	27.5	— 6.5	6.64	0.241	5.65	0.205	0.98	0.036	6.63	0.241	5.66	0.206	85.2	0.01	0.004	0.2	+ 14
G. C.	M	10	26.0	— 7.5	9.19	0.353	7.68	0.295	0.36	0.014	8.04	0.309	8.83	0.340	96.1	1.15	0.044	12.5	+ 43
H. K.	M	10	21.6	— 9.3	7.07	0.327	5.98	0.277	0.65	0.030	6.63	0.307	6.42	0.297	90.8	0.44	0.020	6.2	+ 14
Average		10.4	26.1	— 7.0	7.88	0.303	6.27	0.242	0.82	0.031	7.06	0.272	7.06	0.272	89.1	0.82	0.031	9.2	+ 28
Over 10 Per Cent Underweight																			
K. Bo.	F	8	20.2	—12.2	6.01	0.298	4.54	0.225	0.60	0.030	5.14	0.255	5.41	0.268	90.0	0.87	0.043	14.5	+ 29
F. B.	F	10	17.5	—14.7	5.53	0.316	4.58	0.262	0.72	0.041	5.30	0.303	4.81	0.275	87.0	0.23	0.013	4.2	± 00
E. S.	F	4	12.7	—15.9	5.13	0.404	4.05	0.320	0.34	0.027	4.39	0.346	4.79	0.377	93.4	0.74	0.058	14.4	+ 29
L. B.	F	11	25.1	—20.1	7.37	0.294	5.58	0.222	0.85	0.034	6.43	0.256	6.52	0.260	88.5	0.94	0.037	12.8	+ 43
A. B.	F	6	16.4	—20.4	5.56	0.339	3.23	0.197	0.87	0.053	4.10	0.250	4.09	0.286	84.4	1.46	0.089	26.3	+ 71
A. G.	F	10	22.2	—22.9	5.45	0.245	4.53	0.204	0.73	0.042	5.46	0.246	4.52	0.204	82.9	—0.01	—0.005	— 1.8	± 00
A. G.	F	10	20.1	—28.7	5.55	0.276	4.22	0.210	1.22	0.061	5.44	0.271	4.33	0.215	78.0	0.11	0.055	9.9	+ 43
Average		8.4	19.2	—19.3	5.80	0.310	4.39	0.234	0.79	0.041	5.18	0.275	5.01	0.269	86.3	0.62	0.041	11.5	+ 31

None of the undernourished children lost weight on this diet. Two of them remained stationary in weight and all of the rest made positive gains, although this gain amounted to only about 30 per cent of the gain made on the high protein diet.

As has been already noted, we planned to make our high and low protein diets equal in caloric value. Unfortunately, this was not possible in all cases, since all of the children did not eat the same amount of food. We have, however, a group of eight children who were used as subjects in both experiments and who had practically the same caloric intake. Where there are any differences, they are in favor of the low protein diet. We have therefore assembled the data concerning these children in table 5, which shows the difference in calory and nitrogen intakes on both diets, the calory and nitrogen loss in urine and feces, the nitrogen retention, the ratio of calories to nitrogen, the percentage utilization of calories and the variation in weight.

Table 5 shows, as do the previous tables, that the caloric loss, both in urine and feces, is higher in children on the high protein diet than on the low. The difference in the heat loss in the urine on the two diets is remarkably constant, the caloric value per kilogram of body weight of the urine in children on the high protein diet being, with the exception of two cases, either 1 or 1.1 calories higher than on the low protein diet. The differences in nitrogen output on the two diets may be considered to be largely due to a difference in the concentration of urea. The average difference in urinary nitrogen on these diets is 0.239 Gm. of nitrogen, which represents a difference of 0.51 Gm. of urea, the caloric value of which would be 1.29 calories. It is evident, therefore, that the higher caloric value of the urine in children on the high protein diet is due to the higher concentration of nitrogenous substances, chiefly urea, in the urine on this diet. It may be said, therefore, as has been noted in a previous paper, that when the protein intake is constant the caloric loss in the urine is also remarkably constant, and that the caloric value of the urine is chiefly dependent on the concentration of nitrogenous substances contained in it.

Table 5 shows even more strikingly than the others the differences between the ratios of calories to nitrogen in children on the two diets. On the low protein diet, the ratio is considerably higher than on the high, and the higher the ratio the greater is the difference on the two diets.

The calories lost through the feces are also higher in children on the high protein diet than on the low. Since the percentage absorption in subjects on the two diets is nearly constant, it follows that on a higher protein intake the actual loss through the feces would be greater than on a low intake.

TABLE 5.—*Relation of Protein Intake to Gain in Weight*

Subject	Weight		Intake per Kilogram				Output per Kilogram								Caloric Utilization		Nitrogen Retention per Kilogram		Gain in Weight per Day		Ratio of Calories to Nitrogen	
							Calories				Nitrogen											
							Urine		Feces		Urine		Feces									
	Kilo	Variation from Normal Percent	Calories High	Calories Low	Nitrogen High Gm.	Nitrogen Low Gm.	High	Low	High	Low	High Gm.	Low Gm.	High Gm.	Low Gm.	High per Cent	Low per Cent	High Gm.	Low Gm.	High Gm.	Low Gm.	High	Low
K. B.	20.6	— 4.2	80.0	80.3	0.586	0.308	3.3	2.3	4.6	2.9	0.484	0.255	0.055	0.035	90.0	93.5	0.047	0.018	+ 71	+14	6.9	9.0
G. C.	26.5	— 6.4	78.6	91.2	0.661	0.353	3.1	2.1	4.1	1.3	0.527	0.295	0.044	0.014	91.4	96.3	0.090	0.044	+ 71	+43	5.9	7.0
W. K.	28.6	— 5.5	76.3	78.9	0.632	0.347	2.9	1.8	3.0	2.4	0.495	0.237	0.054	0.034	91.7	94.7	0.083	0.076	+100	+57	5.9	7.6
H. K.	21.7	— 9.1	80.0	79.9	0.633	0.327	3.8	2.3	3.6	2.6	0.495	0.277	0.037	0.030	90.7	95.0	0.101	0.020	+ 86	+14	7.7	8.4
K. Bo.	20.4	—11.4	80.3	81.7	0.644	0.298	3.9	2.9	5.0	2.1	0.470	0.225	0.068	0.030	89.0	93.4	0.106	0.043	+ 71	+29	8.4	12.8
E. S.	13.2	—13.0	76.3	92.0	0.666	0.404	3.7	2.6	2.6	2.4	0.532	0.320	0.035	0.027	91.7	94.7	0.100	0.058	+114	+29	7.0	8.2
F. B.	17.7	—14.0	81.3	81.9	0.583	0.316	4.3	3.0	4.1	3.5	0.522	0.262	0.049	0.041	89.7	92.0	0.012	0.013	+ 43	±00	8.3	11.4
L. B.	25.5	—19.0	81.0	81.0	0.632	0.294	3.9	2.9	4.5	2.3	0.436	0.222	0.063	0.034	89.7	93.5	0.133	0.037	+100	+43	9.0	13.1
Aver.	21.8	—10.3	79.2	83.4	0.630	0.332	3.6	2.5	3.9	2.4	0.557	0.292	0.051	0.031	90.5	94.1	0.084	0.039	+ 82	+29	7.4	9.7

It is interesting to notice that the percentage utilization of the calories of the diet is greater in the case of the low protein than in the case of the high, the average percentage utilization on the low diet being 94.1, and on the high, 90.9. Doubtless this is due to the lower coefficient digestibility of protein as compared with carbohydrate or fat. The lower the protein content of the diet, therefore, other things being equal, the higher the coefficient of digestibility of the mixture, and the greater the caloric utilization.

In spite of the fact that the children selected for comparison in table 5 had either an equal caloric intake, or a higher caloric intake on the low protein diet, and granting that the period of observation of the gain in weight on these diets was short, nevertheless, the gain in weight is strikingly high during the high protein period. All of these children gained during both periods, but, without exception, the gain was from two to three times as high on the high protein diet as it was on the low protein diet. We have also compared the gain in weight during these periods with the gain in weight over an equal period of time on our normal diet, which contained approximately 3 Gm. of protein per kilogram of body weight. On this diet, the normal children gained an average of 18.6 Gm. in twenty-four hours, and the corresponding figures for the four groups of undernourished children were 33.1, 29.1, 44 and 20.8, respectively. Of the eight children on the high protein diet, only one gained as little as 43 Gm. in twenty-four hours, and all the others gained within a range of from 71 to 114 Gm. a day.

These results seem at first glance to be contrary to those of Bartlett,[6] who found that diabetic children could be made to gain at a normal rate for a period of from four to eight months, at least on diets containing as little as from 0.6 to 1 Gm. of protein per kilogram of body weight, provided that the diet was properly adjusted as to its caloric and vitamin content. It must be borne in mind, however, that these children were more or less undernourished at the beginning of the period of observation, and had been undergoing a period of increased protein metabolism and therefore protein depletion as a result of the presence of the disease. For this reason they were able, as were the undernourished children in our study, to use the low protein content of their diet more efficiently than normal children would be. In other words, they were able to retain more of the protein of this limited diet than normal children would be, because the nitrogen content of their bodies was low. It must also be pointed out in this connection that the undernourished children studied by us made what would generally be considered a normal gain even on the low protein diet. But since the

6. Bartlett, W. M.: Protein Requirement as Determined in Diabetic Children, Am. J. Dis. Child. **32**:641 (Nov.) 1926.

gain was more than doubled on the high protein diet, it seems to us to be unquestionably true that a high protein diet is distinctly favorable to growth, especially in the case of the undernourished child. It is a fortunate circumstance that diabetic children, especially at the beginning of treatment, can be made to gain on a limited protein diet, but it would not seem wise or advisable to limit normal children to the same protein intake.

It also seems highly probable that the beneficial effects of the addition of milk to the diet of the undernourished child are due in large part to the increase in the quantity of protein of excellent quality. Our high protein diet contained 1 quart of milk plus a small amount of egg and meat. We believe that the results of this experiment indicate that this amount of milk is necessary for optimum growth, not only because of its high calcium and vitamin content, but also because of the quantity and quality of protein which it contains. We also believe that, especially in the case of the undernourished child, a diet containing as much as 4 Gm. of protein per kilogram of body weight is to be recommended.

An examination of our figures will show that there is the same relationship between the nitrogen intake and the nitrogen retention on both the high and the low protein diets, and that only a small proportion of the nitrogen is retained in any case. The fact that so large a protein intake is necessary for a comparatively small retention is rather difficult to explain. Probably, however, the explanation is to be found in the amino-acid content of the protein. Although we are accustomed to thinking of milk as one of the most adequate of the animal proteins, it is possible, if not probable, that, as in the case of animals, it contains insufficient quantities of certain amino-acids that are essential to the manufacture of certain of the body proteins, and that therefore it is necessary to include what seem to us like large amounts of protein and therefore an excess of less essential acids in the diet in order to secure a sufficient quantity of these limiting amino-acids.

Definite tests were not made, but so far as we could tell from the general appearance and behavior of the children, and also because we observed the same relationship between the intake and output of nitrogen on both diets, although the low protein diet followed the high, we believe that the high protein diet does not have any harmful effects on the children.

SUMMARY

A study of the caloric and nitrogen balance of normal and undernourished children on high and low protein diets shows the following results:

1. The caloric loss in the urine varies directly with the protein output and therefore with the protein intake.

2. The ratio of calories to nitrogen in the urine also varies directly with the protein intake.

3. Nitrogen retention is directly proportional to nitrogen intake.

4. The percentage utilization of the calories in a person on the low protein diet is greater than in one on the high protein diet, owing to the higher coefficient of digestibility of the food mixture of the low protein diet.

5. Underweight children seem to utilize the nitrogen of a low protein diet more efficiently than do normal children.

6. A striking gain in weight follows an increase of the protein in the diet, even in normal children. This is especially marked in undernourished children.

7. A diet containing 4 Gm. of protein per kilogram of body weight is recommended for undernourished children.

8. It is also recommended that the diet of all children, normal or underweight, should contain 1 quart of milk. This is necessary on account of the protein content of this food as well as on account of its content of calcium and vitamins.

SCARLET FEVER

VI. THE USE OF SCARLET FEVER ANTITOXINS *

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Marmarek, in 1895, and Moser, in 1903, produced scarlet fever antistreptococcus serums. Lately, Dochez and the Dicks have introduced their antitoxins or serums. The older therapeutic agents (Moser and Marmarek) were long since discredited because of the intense reactions associated with or following their injections. In this report, we detail our experiences in the use of the recently introduced antitoxins.

METHODS AND MATERIAL

We have used all types of antitoxin—Lilly's unconcentrated, Lilly's concentrated, Dick's antitoxin (received through the courtesy of the Dicks), Lederle's, Squibb's, Parke, Davis and Company's and U. S. Standard Products in more than 700 cases. Because of insufficiency of records, because many of the treated patients were not severely ill, and because many of the patients were treated after the third day of their illness, the records of only 283 patients (moderately or severely ill) are analyzed and compared with 60 normal untreated patients of the same type. The treated as well as the untreated patients had had the disease from four to forty-eight hours before treatment. The period covered was from March, 1925, to Dec. 31, 1926.

We gave patients the antitoxins as they were admitted, approximately every fifth case serving as a control. We considered a patient moderately ill who had a good general rash with a fever of at least 38.5 C. (101.3 F.), an extremely sore throat and signs of general malaise. We considered a patient severely ill who, in addition to the foregoing symptoms, had a fever of 38.5 C. or over with any complication, or who was extremely toxic, or who, while not toxic, was acutely ill.

A record was kept of sickness following the administration of serum and all complications occurring in either the control or the treated patients. In every instance, we tried to ascertain whether or not any previous injections were given such as horse serum, or toxin antitoxin. If there had been any such injection or if there was an allergic background, we ignored the case as far as this series was concerned.

Only thirty-four patients were given injections of the so-called unconcentrated serum manufactured by Lilly's, while all others were given injections of concentrated and refined serums. For convenience, we will term the treated patients, group 1 (283 patients) and the untreated patients, group 2 (60 patients).

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* From the Division of Contagious Diseases, Cleveland City Hospital, and the Department of Pediatrics, Western Reserve University.

RESULTS

Toxicity.—In group 1, there were 134 (47.3 per cent) instances of toxicity varying from mild to severe, while in group 2, there were 25 cases (41.6 per cent). After treatment, this toxicity disappeared, as outlined in table 1. The first line of percentage figures in table 1 represents the percentage of the total number of patients (283 and 60) who lost their toxicity and the time when toxicity was lost, while the second line represents the percentages of toxic patients who lost their toxicity (134 and 25) as represented in hours or days after treatment. The duration of toxicity was less the first few days of group 1 (treated patients), but this difference could not be considered conclusive.

Temperature and Pulse.—The temperature curves drawn in chart 1 show a slightly increased initial temperature in the intramuscularly and intravenously treated patients as compared to the initial temperature

TABLE 1.—*Length of Toxicity*

Number Toxic	12 Hours	24 Hours	48 Hours	72 Hours	96 Hours	5 Days	6 Days	7 Days	Died
Group 1—Two Hundred and Eighty-Three Treated Cases									
	8	71	43	4	3	1	2	2	3
	2.8%	25.0%	15.1%	1.4%	1.0%	0.3%	0.7%	0.7%	1.0%
134									
47.3%	5.9%	52.9%	32.0%	2.9%	2.2%	0.7%	1.4%	1.4%	2.2%
Group 2—Sixty Untreated Cases									
	1	12	7	2	1	2	0	0	0
	1.6%	20.0%	11.6%	3.3%	1.6%	3.3%	0	0	0
25									
41.6%	4%	48%	28%	8%	4%	8%	0	0	0

of the untreated patients. This was due not to the fact that we picked more seriously ill patients for treatment, but because the temperatures in many instances were not accurately obtained before antitoxin was given, as a consequence of which, the first recorded temperature was usually charted after a chill or some other immediate reaction from the serum at a time when it naturally would be extremely high. The chart shows an abrupt drop in temperature and pulse following intravenous injections, but the temperature curve of both intravenously and intramuscularly treated patients is increased above that of the normal untreated patient with scarlet fever at a time when sickness following the use of serum usually comes on, i. e., from about the seventh to the ninth day. The curve of the patients who were treated intramuscularly was not any better than that of the normal untreated person.

At first, the beneficial reactions on the temperature curve following intravenous injections of Dick's antitoxin were definite. The temperature went down and the toxicity disappeared within twenty-four hours in the first fourteen patients who had received injections, and

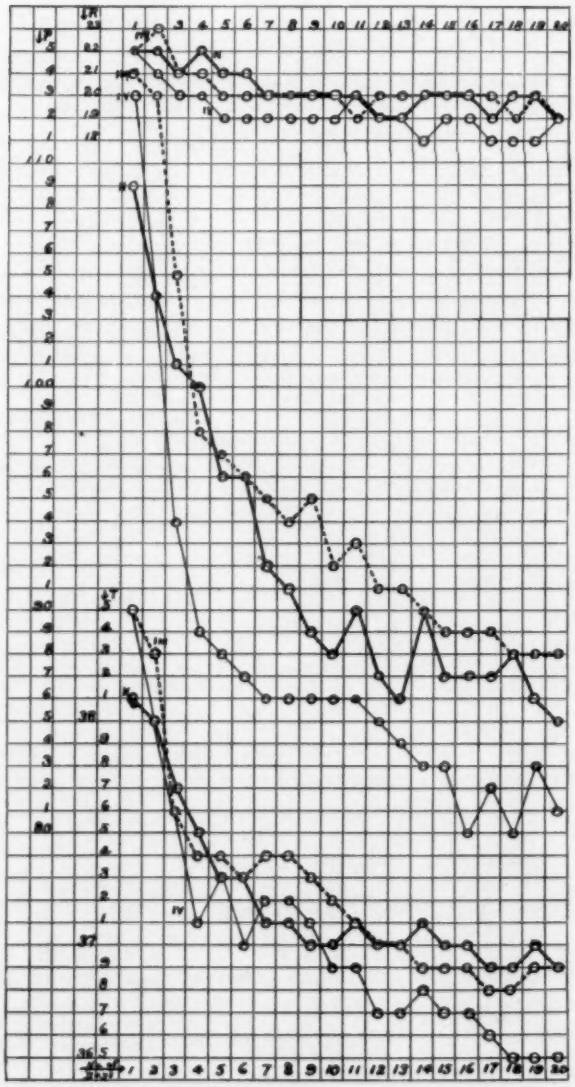

Chart 1.—Response of patients to injections of antitoxin intramuscularly and intravenously as compared to patients untreated by antitoxin. *IM*, intramuscularly, or 229. *IV*, intravenously, or 54. *N*, normal (not receiving antitoxin), or 60.

we attempted to convey an idea of this beneficial reaction in chart 2, figure A. The history of the fifteenth patient who received an injection is as follows.

REPORT OF CASES

CASE 1.—E. C., a boy, aged 6 years, was admitted to the hospital on April 14, 1925, at 4:30 p. m., and died at 4:10 a. m. on April 15. The rash was forty-eight hours old. The temperature was 38.5 C. on admission, and the patient was moderately ill. He was given 20 cc. of Dick's concentrated antitoxin intravenously. Within an hour, the temperature was 41.2 C. (106.1 F.), the pulse uncountable (about 200?) and the respirations around 70. At this time, he had a chill which lasted twenty minutes, and he became comatose. He developed athetoid movements of the hands and feet. The right hand and arm were more spastic than the left hand and arm. The fingers of the hand were drawn back taut. The patient never regained consciousness. He had moisture in the lungs, but we were not certain of the diagnosis of pulmonary edema, although the chest and physical examinations were negative on admission to the hospital.

TABLE 2.—*Effect on Scarlet Fever Rash*

12 Hours	24 Hours	48 Hours	72 Hours	96 Hours	5 Days	6 Days	7 Days	8 Days	9 Days	14 Days	Died
Group 1—Two Hundred and Eighty-Three Treated Patients											
2	33	94	65	38	20	17	5	3	2	1	3
0.7%	11.6%	33.2%	22.9%	13.4%	7.0%	6.0%	1.7%	1.0%	0.7%	0.3%	1.0%
Group 2—Sixty Untreated Patients											
0	4	16	15	11	9	4	1	0	0	0	0
0	6.6%	26.6%	25%	18.3%	15%	6.6%	1.6%	0	0	0	0

Chart 2, figure *B*, gives examples of the temperature curve for the first few days after intramuscular injections, and for comparison, in figure *C* of the same chart, the temperature curves of a few untreated patients are seen.

Effect on the Rash.—The effect of antitoxin on the rash in the two groups is shown in table 2. Twelve and three tenths per cent more patients of group 1 became free from the rash in the first forty-eight hours as compared to the patients of group 2. But this was more than counterbalanced when in the next four days, over 15 per cent of patients of group 2 became free from their rashes sooner than the patients of group 1.

Prevention of Complications.—One hundred and eleven, or 39.2 per cent of the 283 patients, had 129 complications as compared to 22 of the 60 untreated patients, who had 33 complications, or 36.6 per cent. These complications are about the same in type and are listed in tables 3 and 4. If a patient was admitted to the hospital with a serious complication such as meningitis that we knew would be fatal no matter what was done, we did not include it in these tables. If, however, a

patient developed meningitis sixteen days after the administration of the antitoxin, we thought it properly belonged to the complications of a treated group, and it was so recorded. As will be noted in these tables, otitis media and nephritis occur less often in the treated patients, but arthritis and the total number of complications was greater in this group.

TABLE 3.—*Complications* *

Group 1—Two Hundred and Eighty-Three Treated Patients

Complication	Total	Days After Disease Started																				
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
Adenitis.....?	36	1?	..	3	2	5	4	3	3	3	2	2	2	..	1	1	..	..	1	..	..	1	1	1
Adenitis, suppurative 14.1%	4	..	1	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	1	..	1	..	..	..
Anuria	1	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Arthritis, 8.8%	25	..	1	4	..	1	2	4	5	1	2	..	..	..	..	..	..	..	1	1	..	..	2	..
One case the 26th day																								
Furunculosis	2	..	..	..	..	..	..	..	1	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..
Joint abscess	1	..	..	..	..	..	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..
Mastoiditis	4	..	..	..	1	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..
One case the 33d and 38th day																								
Meningitis	2	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	..	..	1	..	..	..	..
Nephritis, 2.4%	7	1?	1	1	..	..	..	..	1	..	2	..	..	..	1	..	..	..	..	..	..	..	..	..
Otitis media, 9.1%	26	3	5	3	2	..	4	..	1	..	..	5	..	..	..	..	..	..	..	..	..	..	..	2
One case the 29th day																								
Paronychia	3	..	..	..	..	..	..	..	1	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..
One case the 24th day																								
Peritonitis	1?	1?	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Peritoneal abscess	3	..	..	1	..	..	..	..	..	..	..	..	1	1	..	..	..	..	..	..	..	..	..	..
Pharyngitis	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1
Pneumonia	2	..	..	..	..	..	..	..	..	..	..	..	1	..	..	..	..	1	..	..	..	..	..	..
Pyelitis	6	2	..	1	..	..	1	..	..	..	..	1	..	..	..	1	..	..	..	..	..	..	..	..
Psychosis	1	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Sinusitis	3	..	..	1	..	..	1	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Ulcerative stomatitis	1	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..

* In addition to scarlet fever, one patient had diabetes and one had measles; neither of these patients died.

TABLE 4.—*Complications* *

Group 2—Sixty Untreated Cases

Complication	Total	Days After Disease Started															
		1	3	4	5	6	7	8	9	12	14	16	18	20	21	22	29
Adenitis, 15%	9	..	2	1	..	1	1	..	..	..	1	1	..	1	..	1	..
Arthritis, 3.3%	2	..	..	..	..	..	..	..	..	..	..	1	..	..	..	1	..
Infected finger	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1
Nephritis, 6.6%	4	1	1	1	..	..	..	..	..	1	..	..	..	..	..	..	..
Otitis media, 15%	9	..	1	4	1	..	..	..	1	..	1	..	1	..	..	..	..
Paronychia	1	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..
Peritoneal abscess	2	..	1	..	..	..	..	1	..	..	..	..	..	..	..	..	..
Pyelitis	2	..	..	..	..	..	..	1	..	..	..	..	..	1	..	..	..
Sinusitis	3	..	1	1	..	..	..	1	..	..	..	..	..	..	..	..	..

* In addition to scarlet fever, one patient had measles.

Serum Reactions.—Ninety-eight (34.6 per cent) patients had late reactions. In addition, 23 (8.1 per cent) patients had early reactions, of which, 12 (6 intramuscularly and 6 intravenously treated) had both early and late reactions, bringing the number up to 109 (38.5 per cent) of 283. Fourteen of the 54 intravenously treated patients, and 9 of the 229 intramuscularly treated patients had immediate reactions. Table

5 gives the time of the reactions of each group, and the length of time that serum sickness lasted is noted in table 6.

An individual reaction may be so hidden in statistics that a true picture is not portrayed. With scarlet fever antitoxin, there are early anaphylactic-like reactions and early thermal as well as late reactions, such as edema of the glottis, persistent hives, pains in the joints, edema of the penis and edema of the tongue. In our experience, the reactions of scarlet fever antitoxin are more marked than those of diphtheria. A short history of three cases illustrates our point.

CASE 2.—R. S., a man, aged 33, was admitted to the hospital on March 10, 1926, and died on March 13. He had been sick four days, and the rash had broken out on the day of admission. He was extremely toxic with a temperature of 39 C. (102.2 F.), and was given antitoxin intramuscularly on admission. The

TABLE 5.—*Early Reactions*

		Minutes and Hours After Injections											
Number of Cases	At Once	2 Min.	5 Min.	10 Min.	15 Min.	20 Min.	30 Min.	40 Min.	60 Min.	90 Min.	2 Hrs.	4 Hrs.	7 Hrs.
23	2	1	1	3	2	1	4	1	3	2	1	1	1

	Late Reactions Days After Injections												
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
98	2	2	3	6	9	13	15	9	7	9	3	9	8	3

TABLE 6.—*Duration of Serum Sickness*

Number of Cases	Number of Days							
	1 or Less	2	3	4	5	6	7	?
90	46	15	17	6	3	1	1	1

temperature went down to normal on March 12. That afternoon, the rash had disappeared. In the evening, the patient had urticaria, and later, about 1 a. m., on March 13, he began to have edema of the glottis. This latter condition became worse notwithstanding treatment and he became more cyanotic and finally unconscious. Intubation was performed, without relief. A low tracheotomy was performed. The patient immediately became conscious and rational again, but died about two hours later.

CASE 3.—J. W., a girl, aged 10 years, was admitted to the hospital on April 11, 1926, and died on April 14. Her illness had begun the day before admission and the rash had broken out on the day of admission. She was severely ill, and nauseated and her temperature was 39 C. Through an oversight, she was not given antitoxin on admission, and the temperature went down to 37.3 C. (99.1 F.) the next day, and the toxicity disappeared. By mistake, she was then given antitoxin intravenously (the day after admission) at 3 p. m. Within an hour, the temperature went up to 39.5 C. (103 F.) and ninety minutes later, she was incoherent, delirious and had an unaccountable pulse. She was still delirious the next day although the rash was disappearing. Constant twitching of the face began

at this time. The rash had practically disappeared by the afternoon of April 13, but the temperature was up to 41.4 C. (106.5 F.). The rash reappeared the next morning, on April 14. The patient never regained consciousness.

CASE 4.—F. J., a woman, aged 31, was admitted to the hospital on May 2, 1926, and died on May 3. She had been ill four days and the rash had broken out two days previous to admission. She appeared moderately ill, and the prognosis looked good, although the temperature was 40.1 C. (105.9 F.). Within an hour after the intravenous injection of antitoxin, the patient had a chill, the pupils became dilated, she became cyanotic and the pulse became rapid, thready and weak and she became semiconscious. Pulmonary edema developed. The patient's neck became stiff. She had clonic contractions of both arms and legs. The twitching continued from 8 p. m., May 2, until 12:10 a. m., May 3, at which time she died.

The experience with cases 3 and 4 was our last with intravenous scarlet fever antitoxin. The reactions thus described occurred in response to injections of various concentrations of antitoxins.

Decrease in Mortality Rate.—Does antitoxin have much influence on the mortality rate? Table 7 shows the mortality rate of the hospital

TABLE 7.—*Scarlet Fever at City Hospital*

Year	Number of Cases	Deaths*	Per Cent
1922	492	15	3.0
1923	760	22	2.8
1924	187	6	3.2
1925	322	9	2.7
1926	644	18	2.7
1927	423	14	3.3
1928	92 (April 1st inclusive)	4	4.3

* Some of these cases came from the metropolitan area outside of Cleveland and would not be included in the statistics of the Cleveland Board of Health.

for patients admitted since 1921. There is a slight reduction in the two years in which antitoxin was used, but if reference is made to the mortality rate of the hospital for 1923, it is found that it is only 0.1 per cent higher. In 1927, we used little or no antitoxin and the mortality rate for the hospital was 0.6 per cent more, but when the individual cases were analyzed, we found that there were enough deaths from virulent diphtheria plus scarlet fever to explain the higher death rate. In fact, if we should exclude the diphtheritic patients who had scarlet fever and who died, the mortality rate would be 1.8 per cent.

It will be noted that the mortality rate for the hospital for 1928, up to April 1, was 4.3 per cent, which would seem to be an increase, but reference to table 8, will show that for the same period of time in the city of Cleveland, the rate was not more than 0.6 per cent, which is less than for 1927, 1926 or 1925. It will be seen, then, that mortality figures from an institution which would sometimes include deaths of residents of other areas than the city in which the institution is located do not lend themselves to comparison without explanation. The mortality rate of the hospital is always higher, as practically 65

per cent or more of the patients who died, died at the hospital. To date, 100 per cent of the deaths in this year occurred at the hospital.

COMMENT

That we had some patients who showed startling improvement after the injection of antitoxin intravenously is certain. This was especially true of the first lot of antitoxin sent us through the courtesy of the Dicks. Our later experience with intravenous antitoxin therapy was not satisfactory on account of the subsequent severe reactions, and as far as the intramuscularly treated patients are concerned, we did not see much difference between them and the untreated patients.

It is often stated that such treatment probably prevents septicemia. It has been our experience that septicemia has not been the most common complication, nor has it always been a fatal one when it has occurred.

TABLE 8.—*Scarlet Fever, Statistics of the Cleveland Board of Health*

Year	Morbidity	Mortality	Per Cent
1912	1,379	90	6.0
1913	1,040	118	11.3
1914	582	48	8.2
1915	928	72	7.7
1916	866	40	4.6
1917	621	14	2.2
1918	408	11	2.6
1919	580	7	1.2
1920	2,257	66	3.0
1921	2,357	119	5.0
1922	2,831	40	1.4
1923	3,653	58	1.5
1924	817	12	1.4
1925	1,004	15	1.4
1926	2,303	33	1.4
1927	1,517	17	1.1
1928	493 (April 1st inclusive)	3	0.6

In any case, it is difficult to conceive how one could definitely conclude that septicemia has or has not been warded off by the use of antitoxins. Such a conclusion must always remain a matter of opinion.

The main objection to the use of antitoxin is that the results are not clearcut and are not conclusive. The benefits of scarlet fever antitoxin are often compared with those obtained from diphtheria antitoxin. The comparison is hard to make since in the case of diphtheria there is a pure toxemia and in scarlet fever there is a toxemia plus the possibility of bacterial infection. When the mortality rate was 25 per cent or more with diphtheria, it was easy to draw general conclusions when that mortality rate went down abruptly after the use of antitoxin. It is hard to see how the mortality from scarlet fever could be any lower.

A second objection to the use of scarlet fever antitoxin is that the patients are made much more ill as a result of the reaction following the administration of serum than they were with the disease. An idea

of the temperature reactions during this sickness from the serum may be had by reference to chart 2, figure 4.

With scarlet fever, the pulse is fast and the heart is often dilated, and all sorts and types of murmurs are found in the early stages of the disease. We do not see the rationale of risking a chill or sickness

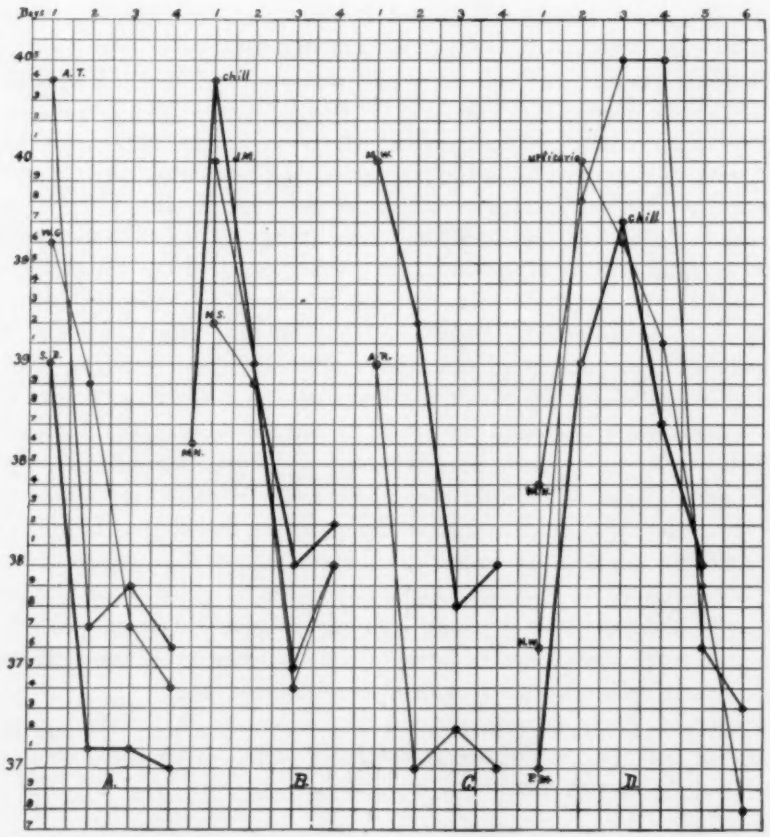

Chart 2.—Temperature curves of patients with scarlet fever. *A*, after intravenous injections of scarlet fever antitoxin. *B*, after intramuscular injections of scarlet fever antitoxin. *C*, antitoxin not administered. *D*, period of serum sickness; *MN*, fourth day after intramuscular injection of scarlet fever antitoxin; *HW*, fourth day after intramuscular injection of scarlet fever antitoxin; *PM*, fifth day after intramuscular injection of scarlet fever antitoxin.

from the use of serum with its coincident rise in temperature and resultant increase in pulse rate in such circumstances.

Active immunization by the injection of the Dick toxin in increasing doses has been most gratifying in our experience and has furnished us a method whereby we have practically wiped out scarlet fever in

our nursing population. We obtain good results with Dick toxin in active immunization, but convincing results are not obtained with the use of scarlet fever antitoxins in treatment. It is hard to reconcile these facts. The two organisms of the Dicks may belong to a group, the active toxin of any one of which can immunize a person against the other strains in the same group. However, the antitoxin made from these strains might not protect or cure a patient who contracts scarlet fever from another strain of streptococcus.

Nothing has been said of the 9 patients who died in 1925 and the ten who died during the first part of 1926, as we have previously analyzed their cases.[1] The patients who died in the latter part of 1926 died for practically similar reasons as those who died in the forepart of the year. If one refers to the reports, it will be seen that close analysis of the individual case brings to light factors that would be little influenced by antitoxin. Indeed, six of the ten patients who died the first part of 1926 received injections of antitoxin within twenty-four hours after the rash had broken out. Even so, we do not classify these deaths as failures of antitoxin treatment any more than we would blame diphtheria antitoxin in case a diphtheritic patient died. There were too many factors to be considered, in cases in which the patients died, to permit the drawing of definite conclusions.

It would seem to us that we might well ask what the practical gain from antitoxin treatment was. Suppose for the sake of argument one concedes the loss of toxicity, of rash, etc., a day sooner after antitoxin treatment! Does this slight improvement which some authors have seen warrant us in injecting into our patients a foreign protein? Is not the treatment somewhat heroic when one remembers the sickness which ensues, following the administration of the serum?

Treatment might be reserved for the extremely ill, but convincing figures do not exist in the literature which would make us think that even in such cases it would do much good.

CONCLUSIONS

1. We present a series of 283 cases in which the patients were treated with scarlet fever antitoxin, and 60 in which treatment was not given.

2. We did not notice any convincing difference in the intramuscularly treated patients as compared with the untreated patients as to toxicity, duration of rash or complications.

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1. Toomey, J. A., and Dolch, E. G.: Studies in Scarlet Fever: III. An Analysis of Scarlet Fever Cases Untreated by Specific Serums or Antitoxins, Am. J. Dis. Child. **33**:424 (March) 1927.

3. Our first fourteen intravenously treated patients showed marked improvement. The remaining forty did not show any marked bettermen as compared to control patients, and three of the forty died in a fashion that was suspiciously anaphylactic.

4. The sickness following the use of serum that has been experienced is extremely severe; in fact, it is usually more severe than the disease itself.

5. We believe that at the present time the evidence in favor of the use of scarlet fever antitoxins is neither clearcut nor decisive.

TUMORS OF THE SPINAL CORD IN CHILDHOOD*

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Incidence
Review of the Literature
Relation of Tumors of the Spinal Cord in Children to Membranes of the Spinal Cord
Age, Duration of Symptoms, Level and Pathologic Diagnosis
Presenting Symptoms
Sensory Changes and Paraesthesias
Bladder and Rectal Disturbances
Effects of Lumbar Puncture
Examination of the Spinal Fluid
Level and Position of Tumor
Preoperative and Postoperative Diagnosis and Operative Results—Mortality
Conclusions

Among 165 verified tumors of the spinal cord for which operation was performed at the Neurological Institute, between 1910 and 1926 inclusive, 8 were found in children 12 years of age or under. Two of the eight children were operated on before 1922, and the remaining six after that date. It is probable that the greater number of cases found in later years is due to the progress made in the recognition of tumors of the spinal cord by the neurologic signs and the information gained by such special tests as the lumbar manometric examination of the spinal fluid, which has now become a routine procedure in all cases in which disease of the spinal cord is suspected. Since the introduction of careful manometric studies of the spinal fluid at the Neurological Institute the number of operations on the spinal cord has increased more than 116 per cent and there has been a corresponding increase in the percentage of cases in which neoplasms of the spinal cord or other forms of obstruction have been found.

REVIEW OF THE LITERATURE

In a review of the literature on tumors of the spinal cord, a relatively small number are found to have been reported in children. It would seem, then, that neoplasms of the spinal cord in children are rare. This view, however, is not supported by postmortem statistics as collected by Schlesinger.[1] Of 251 collected cases of tumors of the spinal cord, Schlesinger found thirty-three occurring before the age of 9 (13 per cent), and twenty-seven between the ages of 10 and 15 (11 per cent).

* Received for publication, July 6, 1928.

* From the Department of Neurological Surgery, Neurological Institute, New York.

1. Schlesinger: Beitrag. z. Klin. der Rückenmarks-und Wirbeltumoren, Vienna, 1898.

Thus, 24 per cent, or nearly one fourth of the series were found in children. Stursburg,[2] in a series of 144 collected cases reported only one in a child under 10 years of age; Schultze,[3] in his series, reported one in a child under 10 years, and niether Nonne [4] nor Flatau [5] (1912) noted any in their collections. Frazier,[6] in his collected statistics, reported four cases, Antoni [7] none and Elsberg [8] one in which the patient was under 10 years of age. This discrepancy between the operative and post-mortem observations suggests that while tumors of the spinal cord do occur in children, they have not, as a rule, been recognized during life.

With more careful neurologic examination and with the aid of special studies, such as the lumbar manometric test, it is probable that in the future statistics will show a greater number of tumors of the spinal cord in childhood that are recognized during life. The neurologic signs are frequently vague, and it is only after special tests have been made that the presence of a tumor is revealed. Some of these cases have been treated as injuries received at birth and others as some obscure disease of the cord, the true condition not being suspected. This is perhaps illustrated by the fact that while within a year after the writer reported an intradural lipoma in a child two additional cases were recognized and reported,[9] up to the time of publication of these cases only nine were to be found in the entire literature. It is possible that among the patients of childrens' hospitals additional cases of tumors of the spinal cord may be found if the possibility of their occurrence is borne in mind and more thorough neurologic examinations and special studies are made.

RELATION OF TUMORS OF THE SPINAL CORD IN CHILDREN TO MEMBRANES OF THE SPINAL CORD

For convenience of study, the tumors of the spinal cord found in children in this series have been grouped in three categories:

Group I, extradural neoplasms mainly within the vertebral canal
Group II, intradural neoplasms
Group III, paravertebral tumors which have invaded the vertebral canal

2. Stursburg: Centralbl. f. d. Grenzgeb. d. Med. u. Chir. **11**:91, 1908.
3. Schultze, F.: Mitt a. d. Grenzgeb. d. Med. u. Chir. **12**:153, 1903.
4. Nonne: Deutsche Ztschr. f. Nervenh. **47**:436, 1913.
5. Flatau: Wirbel-und Rückenmarksgeschwulste, in Lewandowsky: Handbuch der Neurologie, ed. 7, Berlin, S. Karger, 1912, vol. 2.
6. Frazier, C.: Surgery of the Spine and Spinal Cord, New York, D. Appleton & Company, 1918.
7. Antoni, N. R. E.: Ueber Ruckenmarks Tumoren und Neurofibrome, Munich, Bergman, 1920.
8. Elsberg, C.: Tumors of the Spinal Cord, New York, Paul B. Hoeber, Inc., 1925.
9. Personal communication to the author.

Strictly speaking, tumors of the third group should not be included in a series of tumors of the spinal cord. They are mentioned only in passing and will be given but little further consideration in this paper, since they did not present any difficulty in diagnosis. In one, a large tumor of the chest was known to have preceded the signs of cord compression, and in the second case, a large, easily palpable neoplasm of the neck was present with secondary involvement of the spinal cord. Secondary compression of the cord in such cases is obvious and offers no problem in diagnosis.

Those familiar with tumors of the spinal cord will be struck at once by the absence in this series of tumors derived from either the meninges or the nerve roots, especially as arachnoid fibroblastoma and perineural fibroma are the most common varieties of tumors of the spinal cord in the adult. In this group, not a single instance of arachnoid fibroblastoma was encountered.

It was formerly believed that tuberculosis lesions were not infrequently found in the central nervous system. In the statistics collected by Allen Starr,[10] nearly 50 per cent of all the tumors of the brain in children were recorded as tuberculous, whereas the more recent statistics from Cushing's clinic, reported by Van Wagenen [11] show only six of sixteen verified tuberculomas. The records of the Neurological Institute do not show any verified cases of tuberculoma, either intradural or extradural, among the cases in which laminectomy was performed when tumors of the spinal cord were suspected in children. In an interesting case reported by Ash [12] an intradural spinal tuberculoma at the fifth to the eighth cervical segments had been diagnosed during life.

AGE AND DURATION OF SYMPTOMS

The average age of the children in the three groups under discussion is extremely interesting. In the primary extradural group of sarcoma and fibrosarcoma, the average age is 9.2 years, while the secondary extradural group, with the tumor arising outside of the vertebral canal and secondarily invading it, shows an average age of 3 years. In one of the two cases of the latter group, the tumor arose primarily in the thorax or posterior mediastinum, and in the other from the nerves of the neck. The children in the group with intramedullary lesions showed an average age of 11 years. In one of these, however, the duration of the symptoms was apparently more than ten years. In the remaining

10. Starr, A.: Am. J. M. Sc., June, 1895, p. 613.

11. Van Wagenen, W. P.: Tuberculoma of The Brain, Arch. Neurol. & Psychiat. **17**:57 (Jan.) 1927.

12. Ash, R. L.: A contribution to the Diagnosis of Spinal Cord Tumors in Childhood, Am. J. Dis. Child. **13**:487 (June) 1917.

two cases of this group, symptoms had been observed for one and a half years. In the group of cases in which the tumor invaded the vertebral canal secondarily, signs of the spinal cord occurred within a few weeks after the onset of the illness. It would thus seem that a tumor extending secondarily into the vertebral canal may give rise to signs more rapidly than one arising primarily within the vertebral canal itself. This rapid appearance of symptoms may perhaps be explained by the fact that the tumor may have attained considerable size by the time it breaks through the thin eroded layer of bone and suddenly exerts its full pressure on the spinal cord. Tumors arising within the vertebral canal exert their pressure more slowly and gradually on the cord, without any such release of mechanical restraint. Even in the primary extradural tumors, however, there may be a rapid onset of symptoms

TABLE 1.—*Age and Duration: Level and Pathologic Diagnosis*

Case	Age	Level	Pathologic Diagnosis	Duration
Group I: Intramedullary				
H. S.	10 years	Cervical 2-5	Hydromyelia	2 years
P. S.	12 years	Cervical 5-8	Intramedullary tumor	1 year
W. L.	11 years	Cervical 4, thoracic 4	Lipoma	11 years
Average age	11 years		Average duration	4.6 years
Group II: Extradural				
D. M.	9 years	Thoracic 5-7	Sarcoma	6 weeks
H. O.	8 years	Thoracic 4-6	Sarcoma	5 weeks
L. H.	12 years	Cervical 7, thoracic 1	Fibrosarcoma	1 year
Average age	10 years		Average duration	21 weeks
Group III: Paravertebral				
B. D.	3 years	Cervical 4-6	Neurofibroma	8 months
B. M.	3 years	Thoracic 1-3	Sarcoma of thorax	1 year
Average age	3 years		Average duration	10 months

if the tumor shows rapid growth, since expansion can occur more readily at the expense of the cord than of any other tissue in the immediate vicinity. The duration of symptoms in this group was about six weeks in two of the cases and one year in the remaining case.

PRESENTING SYMPTOMS

The presenting symptom in the intramedullary group in one case (P.S.) was pain in the lower part of the back, radiating from both shoulders, followed by weakness of the right arm; in the second case (H.S.), weakness of both legs, followed by pain in the neck and lumbar region; in the third (W.L.), tilting of the head to the right and dragging of the right foot. Though these cases are included in one group, they represent rather widely divergent pathologic processes. Thus, in each instance, though the lesion involved the low cervical segments, the presenting symptoms were extremely variable. Such variability, I believe,

is common in neoplasms of the spinal cord, even when the same segment is implicated. The long fiber tracts are so compactly arranged in the spinal cord that the slightest variation in the exact position in which compression is exerted may mean the implication of a totally different tract and give rise to totally different presenting symptoms.

In one case (W.L.) the tumor probably exerted pressure on the long fiber tracts before involving the ventral horn cells, so that atrophy of the muscles of the upper extremity occurred only later in the course as evidence of involvement of the ventral horn. On the other hand, in another case (H.S.) there was early involvement of the ventral horn cells and tilting of the head to the right due to weakness of the neck musculature was an early sign. In the third case (P.S.) pain radiated over a wider area than would be accounted for by the involvement of the incoming nerve roots, and probably is to be accounted for by implication of the spinothalamic tracts by the pathologic process.

In the extradural group of tumors the presenting symptom in each instance was weakness of the legs. In all three of these cases the tumor was situated ventrolaterally, a position most likely to cause pressure on the pyramidal tracts and on the ventral motor columns. In all three, marked pyramidal tract signs were present, such as the patellar clonus, ankle clonus, Babinski's reflex and absence of the abdominal reflexes. In one case (D.M.), in spite of marked pyramidal signs with double ankle clonus, flaccidity of both lower extremities was present. As observed at operation, the spinal cord in this patient was apparently not markedly compressed or reduced to extreme thinness, as sometimes occurs with large tumors or those of long duration. The relative integrity of the cord was shown by the fairly rapid return of function after removal of the tumor, some return of motor power in the lower extremities being evident at the time of discharge, one month after operation. Spasticity in flexion or in extension is commonly seen in the presence of tumors of the spinal cord, but flaccidity is more usually met with when the cord is markedly compressed, and is, as a rule, to be taken as an indication of an unfavorable prognosis. Flaccidity has been seen occasionally in tumors of rapid growth. The insult to the cord is sudden, and, as in traumatic injuries, manifests itself in flaccidity rather than spasticity. In this instance, the symptoms were of only six weeks' duration, an exceedingly short period for a tumor of the spinal cord. As rapid recovery took place, however, as is usually seen in cases with spasticity. The flaccidity together with the marked pyramidal signs may have misled those who first saw this patient into the belief that they were dealing with an obscure disease of the spinal cord rather than with a tumor.

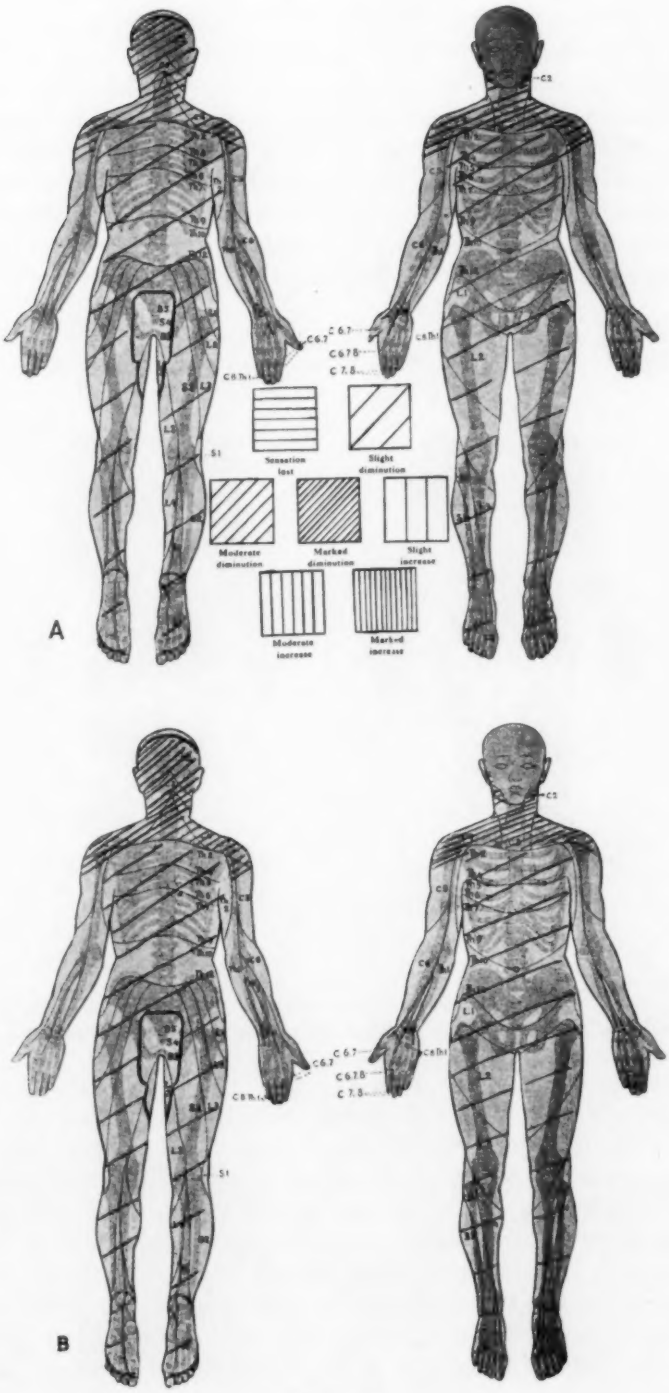
C 6.7
C 6.7.8
C 7.8
C6.7
C6.Th1
S1
Sensation lost
Slight diminution
Moderate diminution
Marked diminution
Slight increase
Moderate increase
Marked increase
A
B

Figure 1

SENSORY CHANGES AND PARESTHESIA

In intramedullary lesions, the sensory changes are likely to be more marked in the dermatomes supplied by the segments at the level of the tumor than in the more distal dermatomes. This is due to the fact that lesions within the substance of the cord, at least in their early stages, interfere with conduction by the segmental and intersegmental fibers of the cord and the crossing pain and temperature fibers which, before they join the spinothalamic tract, may be considered as segmental fibers, though they are actually a part of the long tract fibers. The dorsal and ventral

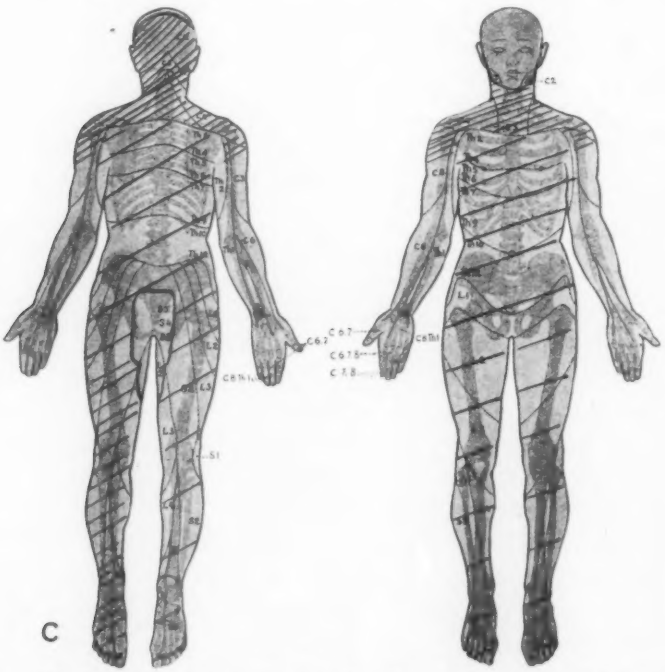

Fig. 1 (H. S.).—Cutaneous sensory disturbances in patient with an intramedullary lesion in the upper cervical segments. *A* indicates tactile sense; *B*, temperature sense, and *C*, pain sense.

muscular masses and their immediate connections are also severely compromised by intramedullary lesions. Hence, it is common to see marked sensory changes at the level of the lesion, with atrophy and fibrillation of the muscles supplied by the segments involved. The more marked sensory changes in the more proximal dermatomes are shown in figure 1. Because of the character of the intradural lipoma it was not possible to determine its exact relation to the cord and to ascertain definitely whether it had invaded the cord secondarily or had arisen primarily within the cord. In any case, at the time of operation it was an intra-

medullary as well as an extramedullary neoplasm. The neurologic signs would seem to indicate that the cord had been invaded secondarily, since the sensory changes resembled more closely those seen in extramedullary than in intramedullary lesions (fig. 2).

In two of the group of extradural tumors a definite sensory level, such as is seen in extramedullary lesions, was found, typically seen in figure 3, but in the third (H.O.), in spite of the presence of a tumor 3 by 5.2 cm. in size pushing the cord markedly to one side, no sensory changes in any modality could be elicited. The only suggestive

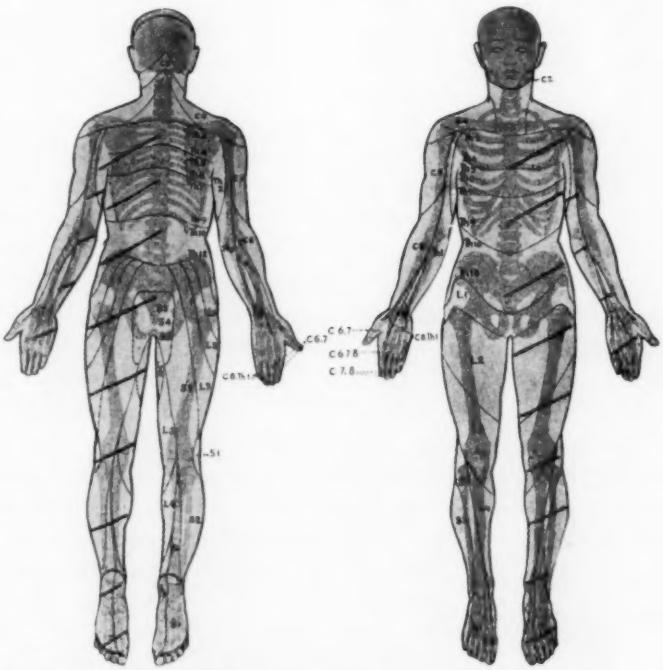

Fig. 2 (W. L.).—Cutaneous sensory disturbances in patient with an intradural lipoma extending from the fourth cervical segment to the fourth thoracic segment.

sensory signs appeared during the week immediately preceding operation when the patient complained that on sitting down the left leg "went to sleep," but no sensory level appeared even after lumbar puncture. The position of the tumor was determined by atrophy in the left shoulder girdle and extensors of the wrist and fingers. In the other two tumors of the extradural group, the sensory changes showed rather definite levels, with nothing remarkable except that in one (D.M.) pain and temperature disturbances were more marked on one side, whereas the motor signs were greater on the opposite side, which was taken to indicate a lateral position of the tumor.

It is interesting to note that none of the patients in this group complained of pain, though until the reports of Nonne,[13] Flatau,[5] Panski [14] and Collins and Marks [15] pain was considered an important presenting sign in tumor of the spinal cord. Since then numerous examples of these tumors without pain have been seen. Pain of long duration referred constantly to one or two segments may serve to indicate that the tumor arises from a nerve root, though pain referable to one side of the body or to the greater part of an extremity is not uncommonly seen as a result of pressure on the spinothalamic tracts. The character of the pain thus produced is different from that due to compression of nerve roots alone. When the spinothalamic tract is compressed, perversion of sensation is more likely to occur, especially the feeling of extreme cold or of extreme heat. Compression of the pain pathway may give rise to perversions of sensation not unlike those seen when a cerebral tumor compresses the thalmus.

Local pain over the vertebral column, either overlying the tumor or elsewhere, was not present spontaneously in any of the tumors of the intramedullary or of the extradural group, nor could it be elicited by movement or pressure on the vertebral column, and this in spite of the fact that in all three extradural cases some abnormality of the vertebrae was found at operation in the region of the tumor. In two of the extradural group a slight degree of scoliosis was revealed by x-ray examination and in the third (L.H.) erosion of the vertebrae with enlargement of the intervertebral foramen was noted. At operation considerable thinning of the vertebral arches was seen, with enlargement of the vertebral canal. The importance of these features—regional scoliosis and enlargement of the vertebral canal—in the presence of the tumors of the spinal cord has been stressed in an earlier paper.[16]

BLADDER AND RECTAL DISTURBANCES

As a rule, incontinence of the bladder and rectum is seldom seen when the tumor of the spinal cord is above the sacral segments unless marked sensory changes are present. Usually, with sufficient pressure to cause disturbance of the rather centrally placed visceral afferent path, all forms of sensation are implicated. In short, when the lesion is above the sacral segments, bladder and rectal incontinence is, generally speaking, evidence of marked compression of the cord. Thus, in one of the

13. Nonne: Neurol. Centralbl. **27**:749, 1908.

14. Panski: Neurol. Centralbl. **31**:1208, 1912.

15. Collins and Marks: Am. J. M. Sc. **149**:613 (June) 1915.

16. Stookey, Byron: A Study of Extradural Spinal Tumors, Arch. Neurol. & Psychiat. **12**:663 (Dec.) 1924.

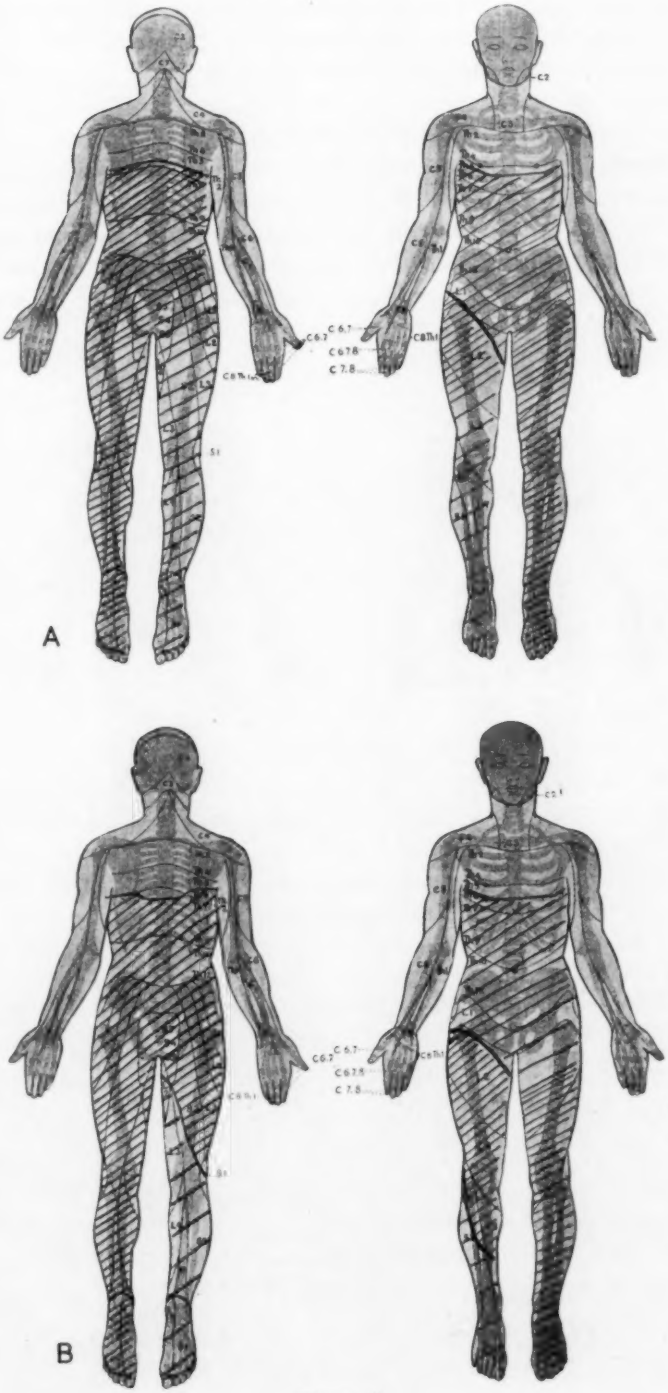

Figure 3

patients in the extradural group incontinence was present, and in another urgency and frequency, but in only one of the intramedullary group was there any disturbance in bladder function.

EFFECTS OF LUMBAR PUNCTURE

Changes in the pressure effects of extradural tumors are likely to take place after lumbar puncture, due to withdrawal of the spinal fluid buffer from between the dura and the cord, which allows the tumor to exert direct pressure on the cord. In one of the patients in the extra-

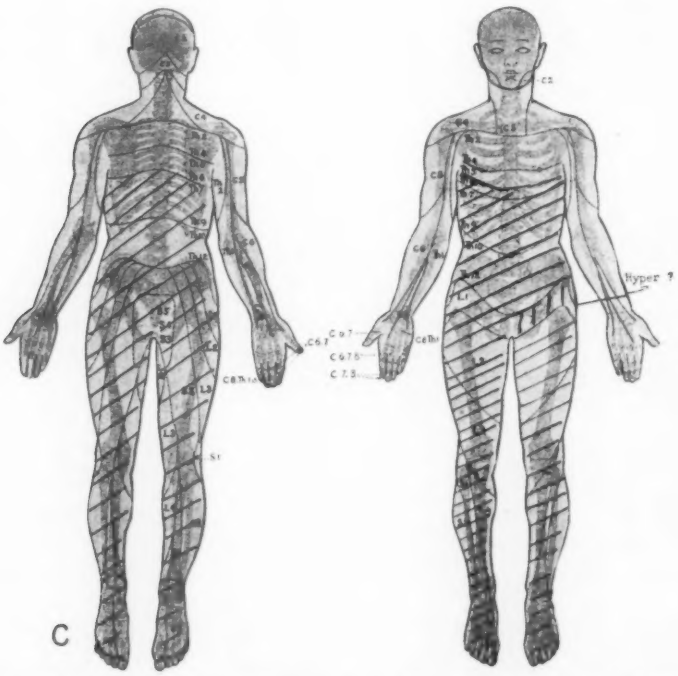

Fig. 3 (D. M.).—Cutaneous sensory disturbances in a patient with an extradural sarcoma with compression of the spinal cord. *A* indicates tactile sense; *B*, temperature sense, and *C*, pain sense.

dural group accentuation of the sensory signs occurred, and in another an increase in the motor signs to such an extent that the little movement previously retained was completely lost. Thus, as pointed out by Elsberg and Stookey,[17] exaggeration of the symptoms following lumbar puncture may be an important sign in establishing the diagnosis of tumor of the spinal cord. Withdrawal of spinal fluid may be used to

17. Elsberg, Charles, and Stookey, Byron: The Mechanical Effects of Tumors of the Spinal Cord, Arch. Neurol. & Psychiat. **8**:502 (Nov.) 1922.

determine a doubtful sensory level, and in a few instances evidence of a sensory level may be obtained which could not be located prior to withdrawal of the spinal fluid. Absence of change in the symptomatology, however, cannot be interpreted as ruling out the presence of a tumor. In one of the patients in this group, sensory changes could not be elicited or a level established even after lumbar puncture. With a symmetrical enlargement of the spinal cord, due either to the tumor or to fluid within the substance of the cord, as occurs in intramedullary tumors, withdrawal of fluid would not theoretically seriously alter the mechanical relations of the cord and the growth. Consequently, lumbar puncture in the intramedullary group is not likely to give rise to changes in the neurologic signs or to the appearance of new symptoms as it is in extramedullary or extradural tumors.

TABLE 2.—*Results of Examination of the Cerebrospinal Fluid*

Case	Color	Cells	Total Protein	Globulin	Colloidal Gold Test	Wassermann Test	Manometric Examination
Intramedullary							
P. S.	Yellow	1	Not done	4+	0-0	Negative	Complete block
W. L.	Yellow	0	Not done	4+	Not done	.....	Complete block
H. S.	Clear	0	15 mg.	0	0-0	Negative	Suggestive block
Extradural							
D. M.	Yellow	5	Not done	4+	0	Negative	Not done (1922)
H. O.	Clear	0	Not done	3+	0	Negative	Complete block
L. H.	Clear	0	Not done	1+	Not done	Negative	Not done (1912)

RESULTS OF EXAMINATION OF SPINAL FLUID

The results of the examination of the spinal fluid are seen in table 2. Thus xanthochromia was present in two cases of intramedullary tumors and in one extradural tumor. In each instance in which xanthochromic fluid was found, a 4+ globulin was obtained. It would seem fair to say that xanthochromia is not seen unless there is a marked increase in the globulin and total protein content of the spinal fluid. Unfortunately, the estimation of the total protein content, as done by Ayer and Fremont-Smith, was not carried out in all our patients, since this method was not then in use. This estimation is now a routine procedure, without which examination of the spinal fluid cannot be considered complete. Xanthochromia has been a rather rare condition at the Neurological Institute in recent years, probably owing to the fact that the diagnosis of neoplasm of the spinal cord is made earlier than it formerly was—thanks both to the advances in the neurologic examination and to the lumbar manometric tests. It is interesting to note that xanthochromia was present in three of the six cases here reported.

The lumbar manometric examination of the spinal fluid has yielded invaluable data. Two of the patients at the Neurological Institute were examined before the manometric examination was in use. In the

remaining four, a positive block was found in three, and a suggestive block in one. In two of the patients the manometric examination was of immense value, for without it a diagnosis of some obscure disease of the spinal cord would have been made. In one of these—in the extradural group—no sensory changes of any kind could be elicited, and in the other the sensory changes, the neurologic signs and the mode of onset were considered too vague to warrant the diagnosis of tumor of the spinal cord. In view of the positive lumbar manometric observations, however, a correct diagnosis was possible (figs. 4, 5 and 6).

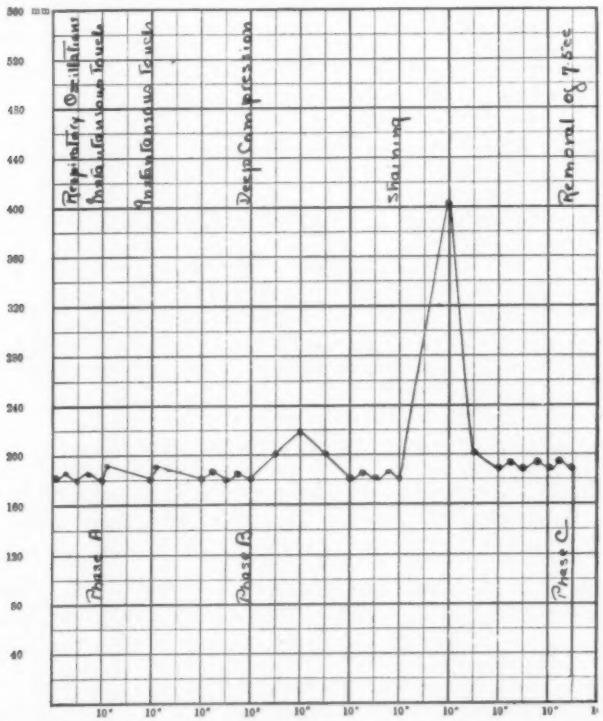

Fig. 4.—Cerebrospinal fluid manometric chart showing complete subarachnoid obstruction obtained by lumbar puncture; positive in all phases. Respiratory oscillations are seen. Instantaneous touch compression is referred to as phase A, and deep compression, as phase B. After phase B, the patient is told to bear down as if to have a bowel movement. Phase C is the pressure level after removal of from 5 to 7 cc. of cerebrospinal fluid. Phase A shows only slight rise and prolonged fall after instantaneous touch compression; phase B, a very slight rise far below normal is seen on deep compression. Phase C shows a marked fall in the cerebrospinal fluid pressure index on removal of 7.5 cc. of fluid.

Routine lumbar manometric studies should be made and the total protein content of the cerebrospinal fluid determined in every child in whom a pathologic process of the spinal cord is suspected.

LEVEL AND POSITION OF TUMOR

It is perhaps significant that all three of the extradural tumors in this series arose primarily on the ventral surface. The exact origin of the so-called extradural group of sarcoma and fibrosarcoma is not known. They appear to be closely attached to the outer layer of the dura, but can always be pealed off readily leaving this membrane smooth and shiny without evidence of erosion. It is probable that tumors of this group arise from the peridural tissue within the vertebral canal, though in some instances they appear to come from tissue outside and

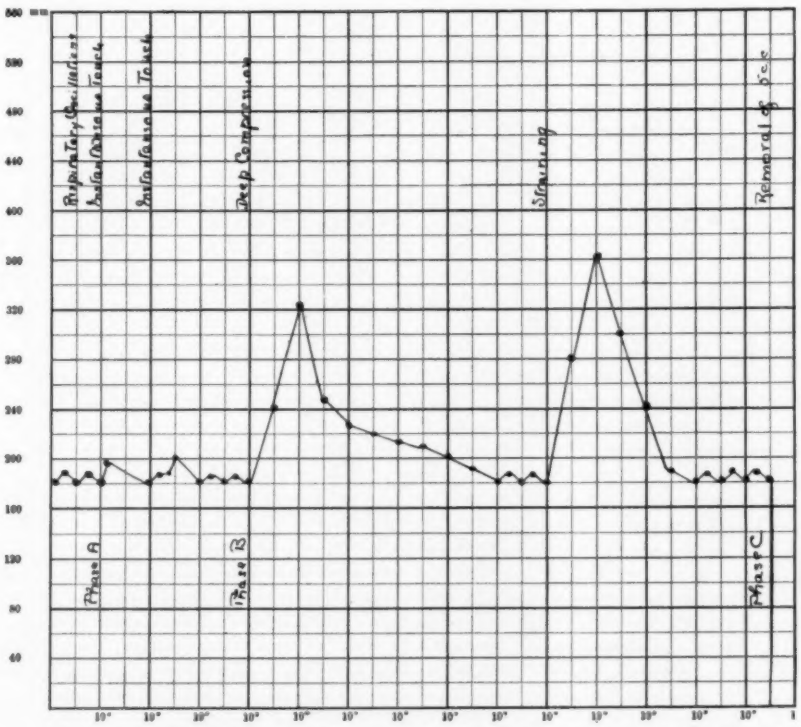

Fig. 5.—Cerebrospinal fluid manometric chart, showing complete subarachnoid obstruction; type II with a prompt rise and delayed fall. Phase A shows a prompt rise but delayed fall; phase B, prompt rise but delayed fall, and phase C, marked fall in spinal fluid pressure on withdrawal of 5 cc. of spinal fluid.

to invade the canal only secondarily. They may be sharply circumscribed and definitely removable; on the other hand, I have seen them surround the dura and extend from the cephalic to the caudal extremity of the vertebral canal. When they are circumscribed and complete removal can be effected the postoperative results are good.

The segmental distribution of the three intramedullary and three extradural tumors is readily seen in table 1. It is interesting to note

that all these tumors occurred in the lower cervical and upper thoracic regions. In my experience, intramedullary tumors are more frequently seen in the cervical region than in any other. This, I believe is suggestive of their congenital origin and is in harmony with the location of such definite congenital lesions as syringomyelia. This latter condition, it is well known, is more commonly seen in the lower cervical segments than in any other part of the spinal axis. Extradural tumors are commonly seen in the cervical region, but are more frequently found in the thoracic region.

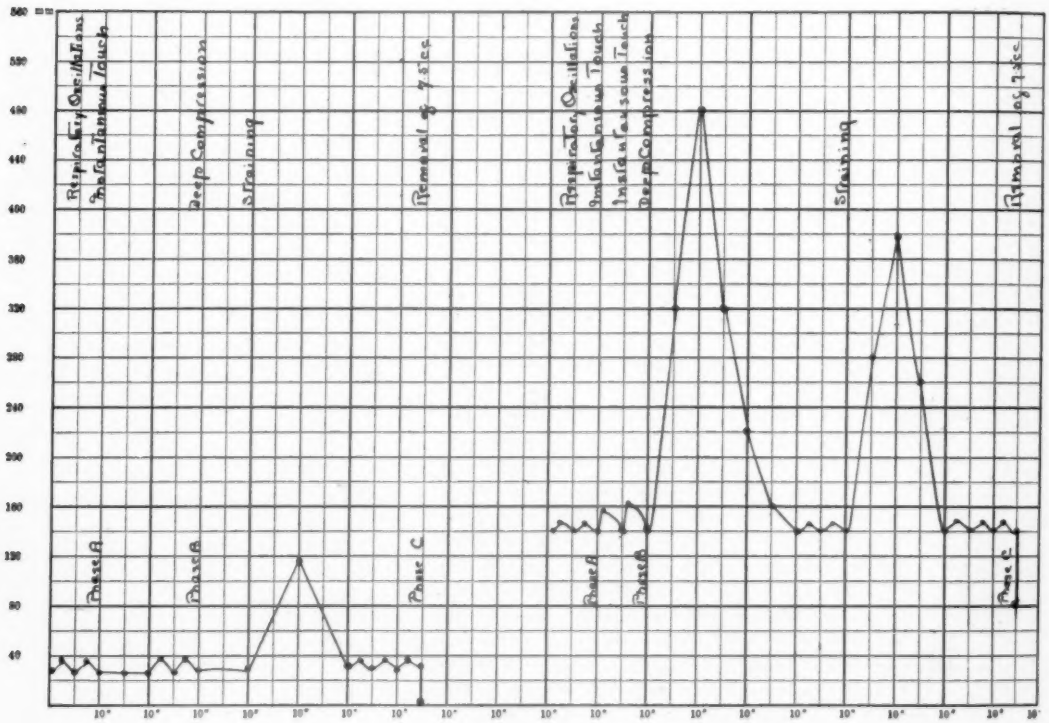

Fig. 6.—Cerebrospinal fluid manometric chart, showing complete subarachnoid obstruction at the left; this type shows initial low pressure. In phase A a rise does not occur on instantaneous touch compression; in phase B a rise does not occur on deep compression, and in phase C there is a fall to zero in spinal fluid pressure on removal of 7.5 cc. of fluid. At the right of the chart normal conditions in a free arachnoid space are illustrated to permit comparison. In the normal chart, phases A and B show a prompt rise and fall. Phase C shows a drop in spinal fluid pressure rarely exceeding from 60 to 80 mm.

PREOPERATIVE AND POSTOPERATIVE DIAGNOSES AND OPERATIVE RESULTS AND MORTALITY

The preoperative diagnoses are extremely interesting. In only one of the tumors of the intramedullary group was a preoperative diagnosis

of intramedullary tumor made. In one, the diagnosis was of intramedullary disease and in another of extradural tumor, thus showing that extradural tumors may frequently give rise to signs closely simulating intramedullary disease. This can readily be understood when it is considered that marked symmetrical compression of a number of nerve roots may occur in extradural tumors and thus give rise to atrophy and segmental sensory disturbances. In the extradural group a preoperative diagnosis was recorded in two of the three cases reported; in only one

Fig. 7.—Patient from whom an extradural sarcoma was removed. On admission she was unable to move her arms or legs. There is no residual paralysis or recurrence.

was it correct. The level of the lesion, however, was correctly diagnosed in each of the cases in which operation was performed, the only variance being in the precise nature of the pathologic process.

In later years, the staff at the Neurological Institute has attempted to make a preoperative diagnosis of extradural neoplasm, extramedullary intradural neoplasm and intramedullary neoplasm. We are aware that the diagnosis of tumor of the spinal cord is sufficient and that attempts

to differentiate the type are not of great advantage, since the exploratory procedure is essentially the same in all. We do feel, however, that when an attempt is made to make a precise differential diagnosis, a more thorough search for minute details will probably be made and that one's diagnostic acumen will be quickened, even though one's vanity may often suffer.

The operative results are, as a whole, gratifying. Even in cases of infiltrating tumors of the intramedullary group which cannot be

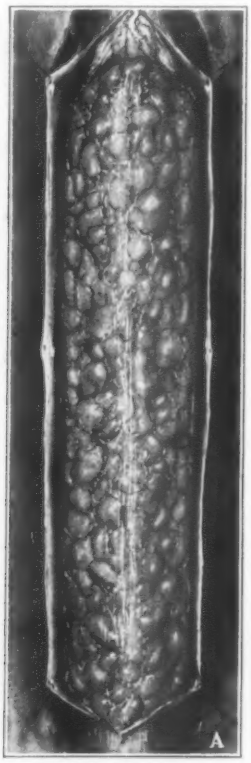

Fig. 8.—Intradural subarachnoid lipoma. The dura was opened and the tumor exposed.

removed, the patients showed improvement. In some the cord can be split and fluid allowed to escape and the dura left open so as to relieve any compression on the spinal cord. In the group of extradural tumors, the results were most satisfactory. Complete recovery was obtained in two of the three patients, and in the third there was relief from all symptoms extending over a number of years and complete relief after a third operation.

It is our present custom to give radiation to all patients in whom extradural sarcoma has been diagnosed, whether or not removal has been apparently complete. It is hoped that thus recurrence may be avoided; this has been the case so far in patients in whom the procedure has been used. In the four cases included in this series freedom from all signs has been obtained, for four years after operation in one case and for two years in the others.

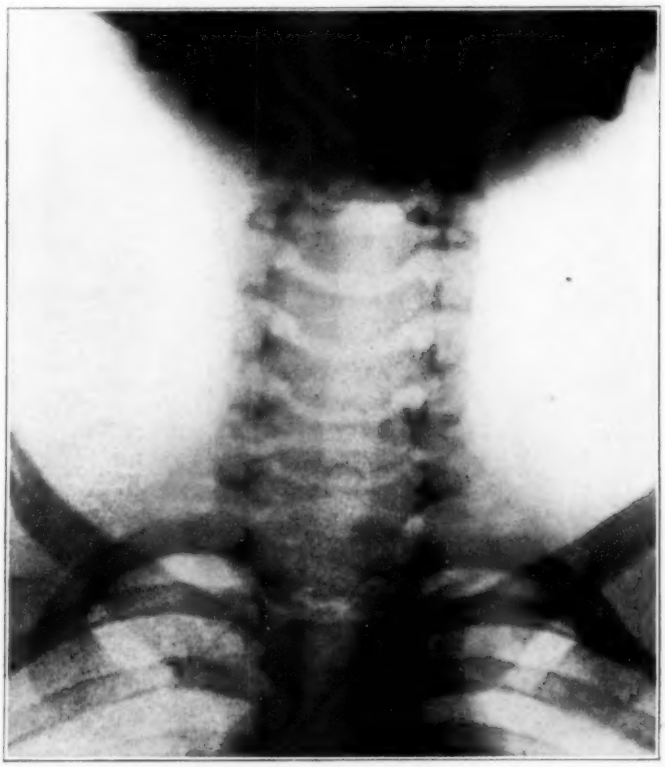

Fig. 9.—Cervical vertebrae showing enlargement of vertebral canal due to subarachnoid lipoma.

Exploratory laminectomy should be performed when there is doubt as to the diagnosis. If care is taken to protect the cord and neurologic technic is employed rather than general surgical technic, the function of the cord should not be disturbed. In the series here reported, death did not occur.

CONCLUSIONS

1. According to the records of verified tumors of the spinal cord at the Neurological Institute, these tumors occur in childhood in about 5 per cent of the cases.

2. While tumors of the meninges and of the nerve roots are most common in adults, they did not occur in the present series in children.

3. Tumors of the spinal cord in children fall into two groups: an intramedullary group and an extradural group. Tumors of the intramedullary group vary in their pathologic process and are likely to be tumors arising from congenital rests within the neural tube. The extramedullary group are usually sarcomas or fibrosarcomas.

Fig. 10.—Spinal cord split in midline between columns of Goll showing intramedullary tumor.

4. The average age of the children in the intramedullary group was 11 years and of those in the primary extradural group 9 years; the group of secondary extradural tumors showed an average age of 3 years.

5. The most common levels were the lower cervical and upper thoracic segments.

6. Extreme variability in the presenting symptom was found, even with tumors in approximately the same segmental level.

7. Pain, either general or localized, was not found over the vertebral column.

8. Bladder and rectal disturbances are rare and occur only late in the history.

9. Lumbar puncture with withdrawal of fluid may be a valuable sign by causing an increase in sensory signs already present, or it may permit a sensory level to be established which could not previously have been determined.

10. The lumbar manometric test has been invaluable. Without it the diagnosis of tumor of the spinal cord would not have been made in 50 per cent of the cases reported. A routine lumbar manometric test should be done whenever disease of the spinal cord is suspected.

11. When there is doubt as to the diagnosis of tumor of the cord, exploration is always indicated. The operative results are satisfactory. Death did not occur in the series here reported.

SO-CALLED IDIOPATHIC ENLARGEMENT OF THE HEART IN INFANCY AND IN CHILDHOOD*

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By idiopathic enlargement of the heart is meant an enlargement of the entire organ or parts of it which cannot be explained on a pathologic basis. I have found in the literature thirty-four cases reported as such which are accompanied by pathologic reports. In five of these, anomalies or abnormalities of the heart necessarily precluded their consideration as instances of idiopathic enlargement. In another case, the kidneys were twice the normal size, and while the microscopic examination did not reveal definite abnormalities, this case too cannot be considered as idiopathic. In five of the remaining twenty-eight cases, histologic examination was not mentioned. In six more, the microscopic examination revealed pathologic conditions in the musculature, and these may not be considered as truly idiopathic.

There remain, then, only seventeen cases which on the basis of anatomic and histologic examinations may be considered as true idiopathic enlargement (hypertrophy) in infancy and in childhood. The case reported was considered idiopathic; histologic examination, however, revealed pathologic changes in the musculature.

REPORT OF CASE

History.—F. M., a boy, aged 15 months, was admitted to the children's service of the Mount Sinai Hospital on April 22, 1927, with the complaint of vomiting of two weeks' duration and cough of one day's duration. The family history was negative. The child had had a birth weight of 9 pounds (4 Kg.) after normal delivery. There was nothing remarkable or untoward in the developmental or nutritional history, and the child was said always to have been well. Two weeks before admission, vomiting had occurred. This had persisted after every meal, although the child was otherwise well and active. There had not been a cough, fever, drowsiness or appearance of illness until the day of admission.

Examination.— On physical examination, the patient appeared pale, dyspneic and acutely ill. There was slight cyanosis. The impression on inspection was that of respiratory involvement. Over the posterior bases of the lungs there were scattered, coarse and crepitant râles and a slight dulness; the breath sounds were exaggerated and faintly bronchial. The heart did not present abnormal conditions. The liver and spleen were palpable a fingerbreadth below the costal margin. Otherwise, abnormal conditions were not found. The tem-

* Received for publication, June 6, 1928.

* From the Department of Laboratories and the Pediatric Service of the Mount Sinai Hospital.

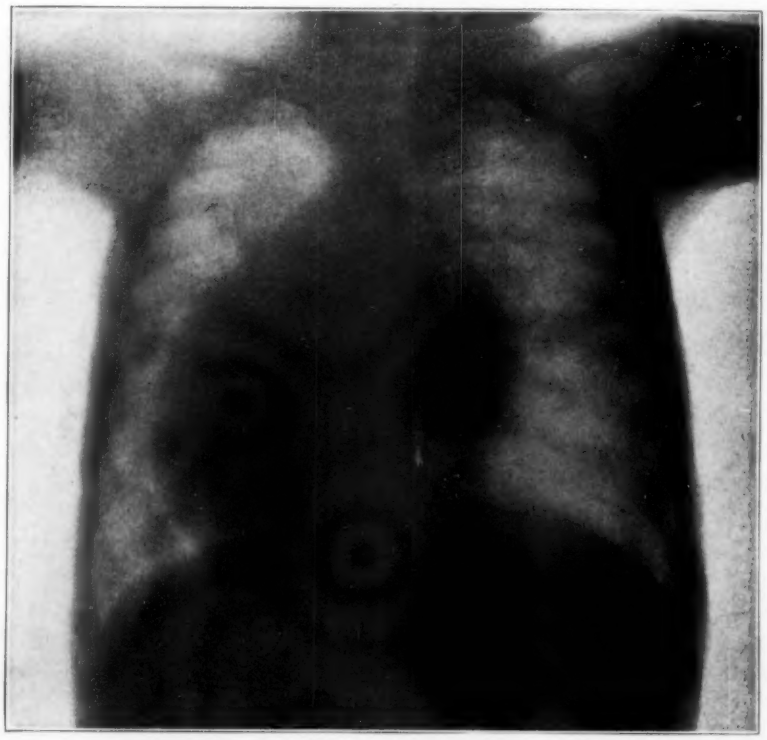

Fig. 1.—Marked enlargement of the heart on both sides but predominately to the left.

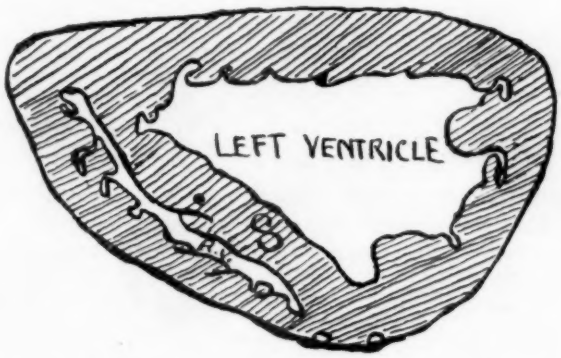

Fig. 2.—Actual size of the heart in cross-section and marked dilatation of the left ventricle and slight hypertrophy of both ventricles.

perature was 100 F., respirations 40, and pulse rate 140. The hemoglobin content (Sahli) was 65 per cent; the total white count, 8,200; polymorphonuclears, 68 per cent; lymphocytes 4 per cent, and mononuclears, 4 per cent. The urine was normal. The roentgen-ray examination on the day of admission showed a marked enlargement of the heart in all directions but most pronounced on the left side, and a globular shape which suggested the possibility of congenital cardiac disease (fig. 1). On the day following admission, the patient died suddenly.

Fig. 3.—Left ventricle posterior, figure 1; lymphocytic infiltration and interfibrillar proliferation of the connective tissue separating the muscle fibers. The myocardium has a patchy appearance; magnification, × 80.

Autopsy.—At autopsy, confluent bronchopneumonia was found in the lower lobe of the left lung and in scattered areas in other parts of the lungs, but none of these was of great extent. There was a purulent bilateral otitis media. The heart showed marked enlargement of both ventricles, the left being so dilated as to constitute two thirds of the volume of the entire organ. The right auricle was small, and the foramen ovale admitted a coarse probe. The inter-

ventricular septum bulged towards the right, making the cavity of the right ventricle appear smaller than normal (fig. 2). The pulmonary valves and artery did not present any abnormalities. The papillary muscles appeared enlarged. The musculature was dark brown and did not reveal any scarring. A narrowing of the aortic arch did not exist, and abnormalities of the aortic valves were not apparent. The weight of the heart was 155 Gm., the average normal for this age being from 37 to 45 Gm. The other valves and the coronary arteries did not show any abnormalities.

Microscopic studies were made from sections taken from the anterior and posterior parts of the left ventricle, several parts of the right ventricle and

Fig. 4.—Left ventricle anterior, figure 1; marked lymphocytic infiltration near the epicardium; magnification, × 80.

interventricular septum, the left auricle and all the valves. These were stained with eosin-hematoxylin and with van Gieson elastica. Examinations for bacteria and spirochete were made, with negative results.

Photomicrographs made under low and high power magnification are herewith presented to illustrate the typical conditions in the heart musculature. Under low power examination, there was an immediate impression of pathologic alteration in the musculature because of its outspoken patchy appearance and the presence of infiltrations (fig. 3). Higher magnification revealed the diffuse

infiltrations to be composed of round cells which were predominantly small lymphocytes and occasionally somewhat larger mononuclear cells (fig. 4). There were generalized areas of degeneration of the muscle: a destruction and fragmentation of the muscle fibers with here and there replacement by loose areolar tissue (fig. 5). In places the muscle fibers were seen to be interrupted and pale, and where there was such an interruption there was a proliferation

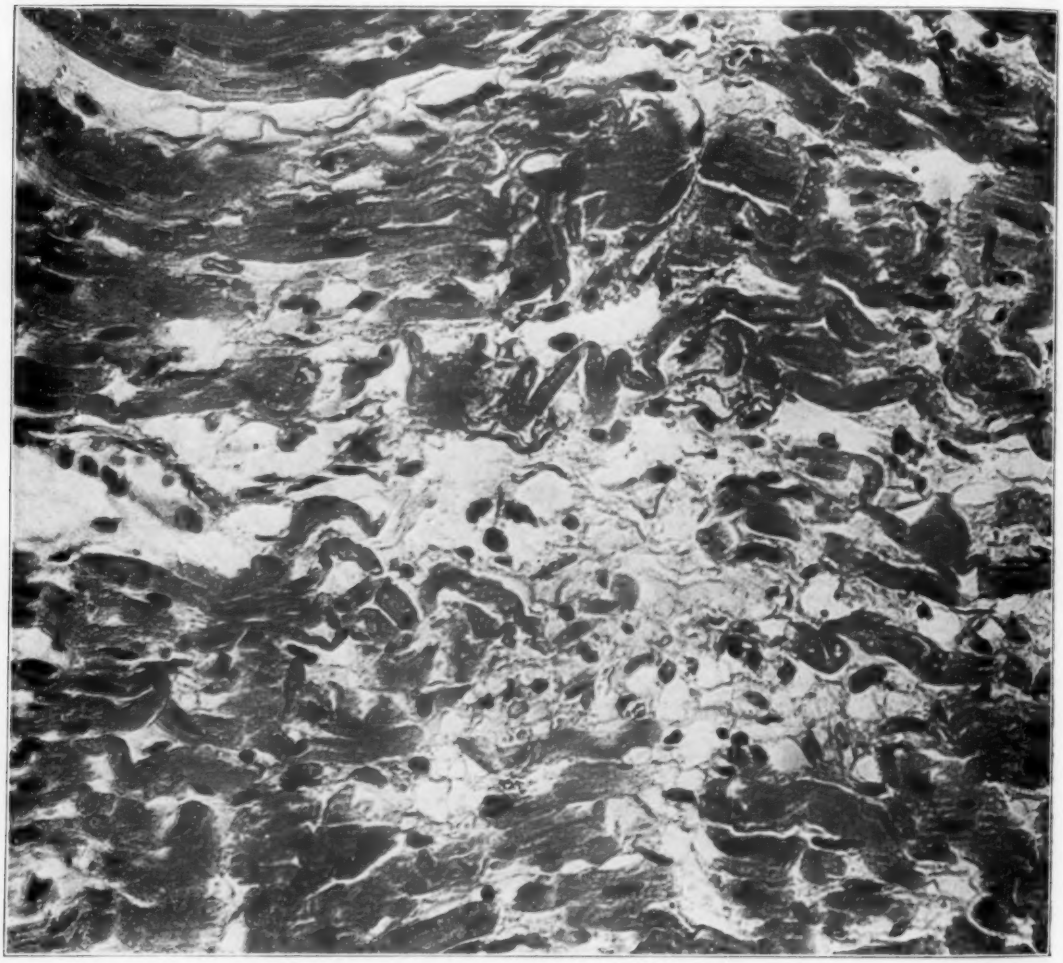

Fig. 5.—Right ventricle, figure 2; area of complete neurosis of the muscle with a few particles remaining; magnification, × 250.

of the perimysial tissue. Occasionally, muscle fibers that were thicker, had very large nuclei, and were apparently hypertrophic were recognized (fig 6). Extravascular exudation of leukocytes was not seen. Only occasionally was there an accumulation of cells around a blood vessel. There were patches showing scattered fragments of muscle and sarcolemma. The inflammatory process

remained within the limits of a diffuse moderate lymphocytic infiltration—a picture which suggested its origin in a primary degeneration of the muscle fibers and a reparative proliferation of the framework of connective tissue of the heart and of the lymphocytes. The valves did not show any abnormalities.

ETIOLOGY

In the accompanying table is given a summary of the significant and relevant positive observations in all the cases I have found in the literature reported as or considered as idiopathic enlargement of the heart in

Fig. 6.—Left ventricle posterior, area at high magnification: groups of lymphocytes and large mononuclear cells. The muscle fibers frequently show degeneration with only residue of the sheaths remaining. There are occasional large nuclei visible indicating hypertrophy of muscle cells.

infancy and in childhood. The term "enlargement" is used advisedly, since the terminology varies, e.g., hypertrophy, dilatation, congenital hypertrophy and cor bovinum are used. It would be better, I feel, to speak simply of enlargement, as it is the most significant qualification which is at once clinical and anatomic.

Summary of Observations on Cases of Idiopathic Enlargement of the Heart in Infancy and Childhood

Author and Periodical	Significant Clinical Facts	Postmortem Observations	Etiology Given by Author
1. Henoch: Beitr. z. Kinderheilkunde p. 239, 1868	Aged 3 months; dyspnea; sudden death	Hypertrophy and dilatation of the heart particularly of left ventricle; thymus enlarged	
	Aged 9 years	Hypertrophy and dilatation of the heart particularly of right ventricle	
2. Rheiner: Virchow Arch. f. path. Anat. **123** : 112, 1891	Aged 3 months; dyspnea, cyanosis, anorexia, large heart; sudden death	Weight of heart, 170 Gm.; diaphragm in left ventricle residual to fetal endocarditis and producing effect of stenosis and insufficiency of mitral valve; hypertrophy left ventricle marked	Congenital giant growth since abnormality, not enough to explain massive hypertrophy
3. Hauser: Deutsche Med. Wchnschr. **22** : 705, 1896	Aged 11 months; severe pertussis, anemia, enlarged heart; sudden death	Weight of heart, 77 Gm.; hypertrophy and dilatation both ventricles, particularly left; beginning fatty changes in heart and kidneys; beginning atrophy trabeculae and papillary muscles of left ventricle	Plethora and stasis in abdomen following severe coughing; and increased pressure in lungs cause hypertrophy
4. Hauser: Deutsche Med. Wchnschr. **25** : 425, 1899	Aged 14 months; dyspnea, cyanosis, weakness, hoarseness; sudden death	Slight aneurysmal dilatation of conus; marked thickening of endocardium in both ventricles so as to be ring formed and to have a stenosing effect on valves opposite; scattered pneumonic patches; histology negative	Congenital
5. Simmonds: München. med. Wchnschr. **46** : 108, 1899	New-born	Weight of heart, 44 Gm.; both ventricles generally hypertrophic; microscopic negative	Congenital; perhaps a circulatory disturbance of unknown nature gone at birth
6. Hueter: München. med. Wchnschr. **47** : 271, 1900	Aged 6 months; sick 6 weeks; enlarged heart, bulging thorax; sudden death	Rickets; hydrothroax; right ventricle filled apex, left looked like appendage; massive hypertrophy right ventricle; pulmonary artery strongly developed; endocardium on conus; pulmonary artery thickened; aorta smaller than pulmonary artery, microscopy not given	Congenital; Simmonds believed it due to congenital narrowing of aorta caused by swelling on septum
7. Paulssen: Inaugural Dissertation Munich, 1901, Kastner	Aged 8 years; cough, bloody sputum, weakness 1 year, large fluid intake	Weight of heart, 135 Gm.; subacute tuberculosis; large ventricles; thick musculature	Large fluid intake
8. Hedinger: Virchows Arch. f. path. Anat. **178** : 264, 1904	Aged 1 year; slow development pneumonia at 11 months; bulging cardia, systolic over cardia, enteritis	Weight of heart, 157 Gm.; hypertrophy of both halves of heart; left lung completely atelectatic; microscopy negative	Hypertrophy secondary to atelectasis of lungs; Wyss considered it idiopathic
	Aged 14 months; discontinued attempts to walk; enlarged heart; faint systolic murmur at base; sudden death	Weight of heart, 190 Gm.; both ventricles enlarged, left more than right; septum bulges into right; endocardium of left ventricle diffusely thickened; thrombus in left ventricle; left lung collapsed; microscopy, hypertrophy of muscle fibers; suprarenals not examined	Either fetal endocarditis or a hypersecretion of the chromaffin system
9. Oberndorffer: Verhandl. d. Gesellsc. f. Kinderh. **23** : 180, 1906	Stillborn	Weight of heart, 40 Gm.; strongly developed auricles; apex built of both ventricles; microscopically, muscle fibers thick and enlarged; slight increase of myocardial interstitium	

Summary of Observations on Cases of Idiopathic Enlargement of the Heart in Infancy and Childhood—Continued

Author and Periodical	Significant Clinical Facts	Portmortem Observations	Etiology Given by Author
	Aged 3 months; cramps; sudden death	Weight of heart, 66 Gm.; entire heart enlarged but left side more than right; in left ventricle, thinning of walls in places almost aneurysmal trabeculae flattened in places like cords; pulmonary artery somewhat larger than aorta; microscopically, enlarged muscle fibers, increased interstitium; thymus enlarged (22 Gm.)	Secondary to alteration in pressure conditions in mediastinum
	Aged 6 months; sick, few days; cramps; sudden death	Weight of heart, 62 Gm.; both ventricles enlarged, left more than right; apex filled by left ventricle; microscopy: muscle fibers thickened, connective tissue increased; slight enlargement of thymus	Possibly the enlarged thymus
	Aged 9 months; suggestion for pertussis; sudden death	Weight of heart, 105 Gm.; marked enlargement left ventricle; microscopy: connective tissue increased	
	Aged 14 months; flaccid paralysis of extremities 4 weeks before death, which was sudden	Weight of heart, 136 Gm.; anterior and posterior walls of left ventricle flattened almost aneurysmal; endocardium of ventricles thickened; pulmonary artery somewhat wider than aorta; microscopy: enlargement of muscle cells and nuclei poliomyelitis and polioencephalitis of brain	Congenital or possibly parental alcoholism
10. Efron, cited by Hedinger (8)	Aged 6 months; bronchitis 2 months previous; enlarged heart	Size, eight times fist of child; apex both ventricles; papillary muscles thickened; left bronchus occluded by heart; microscopy: hypertrophy of muscle fibers	Embryonal giant growth
11. Kaufmann: Cor.-Bl. f. schweitz. Aerzte **36** : 566, 1906	Aged 8 months; cyanotic; moribund	Weight of heart, 142 Gm.; left ventricle enlarged; bronchopneumonia	
12. Michaud: Cor.-Bl. f. schweitz. Aerzte **36** : 779, 1906	Aged 3 years; sick 2 days; dyspnea, ascites, large heart	Weight of heart, 155 Gm.; high grade hypertrophy and dilatation of both ventricles, but left more than right; endocardium of left ventricle thickened; edge of mitral valve slightly thickened; mitral, tricuspid, aortic and pulmonary valvular orifices somewhat enlarged; kidneys show areas of still undeveloped fetal glomeruli; muscle fibers of heart thickened; no microscopic changes of adrenals noted	Excludes renal causes a hypofunction of chromaffin system causing fixation in dilatation and compensatory hypertrophy
13. Riesenfeld: Jahrb. f. Kinderh. **86** : 419, 1917	Aged 11 months; fourth attack, vomiting after meals, cyanosed lips, weakness, large heart, liver and spleen enlarged	Edema of brain; hypertrophy and dilatation of both ventricles, particularly left; very large thymus; swelling of spleen and all lymph glands	
	Aged 11 months; often coughed; dyspnea, cyanosis, groaning, clouded sensorium, spleen enlarged	Status lymphaticus; slight stenosis isthmus aorta; broad aortic arch; anemia	

Summary of Observations on Cases of Idiopathic Enlargement of the Heart in Infancy and Childhood—Continued

Author and Periodical	Significant Clinical Facts	Portmortem Observations	Etiology Given by Author
	Aged 9 months; cough 6 days, sleeplessness, groaning, vomiting, transient cyanosis, heart enlarged, cloudy sensorium	Generalized enlargement of lymph glands (status); hypoplasia suprarenals with barely appreciable marrow; hypertrophy and dilatation both ventricles, especially left; microscopic: lymphocytic infiltration of heart muscles and degeneration of muscle	Lymphocytic infiltration directly caused atrophy; then followed dilatation and compensatory hypertrophy
	Aged 9 months; cough, sneeze, restlessness	Status lymphaticus; edema of brain; marked thymus hyperplasia; hypertrophy and dilatation both ventricles, especially left; purulent foci kidneys; lymphocytic infiltration of heart muscle and myocardial degeneration	Lymphocytic infiltration directly caused atrophy; then followed dilation and compensatory hypertrophy
	Aged 18 months; dyspnea, anorexia, fever	Status lymphaticus; massive thymus enlargement; hypertrophy and dilatation both ventricles, especially left; lymphocytic infiltration of heart muscle and myocardial degeneration	Lymphocytic infiltration directly caused atrophy; then followed dilatation and compensatory hypertrophy
14. Howland: Contributions Medical and Biological Research, New York, Paul B. Hoeber, 1919, p. 583	Aged 2½ years; pertussis, cyanosis, fainting spells, large heart, short systolic murmur at base	Weight of heart, 120 Gm.; right heart greatly hypertrophied and dilated; pulmonary artery dilated; right auricle slightly dilated; right ventricle hypertrophic; microscopy: normal	
	Aged 16 months; irritability, pallor, dyspnea, large heart; sudden death	Weight of heart, 180 Gm.; left thorax bulged, filled almost entirely with heart; both ventricles dilated; slight hypertrophy of muscle fibers	
	Aged 4 years; dyspnea, slight bulging pericardium; high pitched systolic blowing murmur	Weight of heart, 160 Gm.; considerable dilatation, chambers of heart; almost complete displacement of lung tissue, left side	
	Aged 10 months; attacks of dyspnea, fainting spells, apathy, cyanosis, cough, fever; large heart	Weight of heart, 100 Gm.; greatly enlarged heart; thymus enlarged (22 Gm.); microscopy: negative	
	Aged 2 years; breathlessness, dyspnea; heart enlarged; sounds indistinct; stupor for 48 hours	Weight of heart, 110 Gm.; pleural effusion both bases; heart enormously enlarged, particularly to left; apex bifid; left ventricle hypertrophied	
15. Martha Berger: Monatschr. f. Kinderh. **29**: 193, 1924	Aged 2 months; hunger for air; large heart; several attacks of cyanosis; loud systolic murmur at apex	Heart three times normal size; fresh pneumonic patches; microscopy: hypertrophic muscle fibers	Congenital
16. Carrington, G. L., and Krumbhaar, E. B.: So-Called Idiopathic Cardiac Hypertrophy in Infancy, Am. J. Dis. Child. **27**: 449 (April) 1924	Aged 10 months; puny; sick few days; flatness left chest; large heart; died suddenly	Weight of heart, 136 Gm.; right auricle and ventricle hypertrophied; left ventricle greatly hypertrophied and dilated; left coronary artery arose anomalously from pulmonary artery; microscopy showed terminal bronchopneumonia, degeneration of myocardium, slight localized myocardial fibrosis, slight mixed nephritis	Anomaly and slight mixed nephritis not adequate causes for enlargement

Summary of Observations on Cases of Idiopathic Enlargement of the Heart in Infancy and Childhood—Continued

Author and Periodical	Significant Clinical Facts	Portmortem Observations	Etiology Given by Author
17. Bluehdorn: Monatschr. f. Kinderh. **29**: 193, 1925	Aged 1½ years; eczema, dyspnea, cyanosis of lips, slight albumin; sudden death	Status lymphaticus; marked hypertrophy and dilatation of heart, round cell infiltration of heart musculature and atrophy of myocardium, fresh primary tuberculous infection of lungs	Microscopic picture perhaps due to tuberculosis or eczema; author called it myocarditis interstitialis
18. Scott, A. J., and Zeller, A. H.: Congenital Cardiac Hypertrophy, Am. J. Dis. Child. **31**: 31 (Jan.) 1926	Aged 5 weeks; dyspnea, cyanosis on crying, gastrointestinal disturbance; large heart	Weight of heart, 55.4 Gm.; hypertrophy of left ventricle; right auricle dilated	Congenital
19. Krstulovic: Monatschr. f. Kinderh. **33**: 113, 1926	Aged 9 months; premature enlargement of heart noted at 4 months; pallor; cyanosis; dyspepsia; sudden death	Three times normal size; left ventricle strikingly large; endocardium of left ventricle diffusely thickened; microscopic: hypertrophy of muscle fibers	Chronic recrudescing myocarditis
20. Mouriquand, Bortoye and Charlote: Arch. de méd. d. enf. **29**: 83, 1926	Aged 13 months; dyspnea; intense murmur; severe anemia	Weight of heart, 70 Gm.; extremely large heart; hypertrophic left ventricle; histology of heart normal; kidneys large but no microscopic lesions	

Fraetzel [1] listed as causes of idiopathic hypertrophy which come under consideration in childhood: excessive resistance in the pulmonary system, disease of the kidneys, congenital narrowing or congenital excessive size of the aorta, fatty heart, diphtheritic heart and diseases of the cardiac nervous system. Michaud (12 in the table) mentions excessive fluid (beer) intake, scarlatinal nephritis, synechia of the pericardium, infections and anemia. Virchow [2] stated that a diffuse rhabdomyoma may produce a localized or generalized hypertrophy of the heart. According to Mayr,[3] new-born infants may show a congenital hypertrophy of the heart with concomitant enlargement of the thymus, thyroid, liver and spleen without cyanosis and usually with an inflammation of the lungs leading to a fatal issue. He does not cite any cases, however. Henoch (1 in the table) observed two cases which he believes are congenital; in one, the thymus was enlarged. Simmonds (5 in the table) explained the idiopathic hypertrophy in his case by hypothecating some unknown intra-uterine circulatory disturbance present only in early fetal life, which may have disappeared or be unrecognizable at the time of birth. In a series of five cases, Riesenfeld (13 in the table) found a status lymphaticus associated with the enlarge-

1. Fraetzel in Wood: Idiopathic Enlargement of the Heart, 1890, vol. 6, p. 530.

2. Virchow: Klin. Wchnschr. **33**:679, 1896.

3. Mayr: Ausserordentliche Beilage, Jahrb. f. Kinderh. **5**:44, 1862.

ment of the heart, and in two cases the thymus was also enlarged. Ceelen [4] found on examination of the cases of Riesenfeld that the hearts showed a generalized infiltration of predominantly small lymphocytes but also larger ones resembling lymphogonias and lymphoblasts; there were also areas of muscle atrophy and fatty degeneration. Riesenfeld stated the belief that the round cell infiltration is the direct cause of the fatty degeneration and atrophy, and that dilatation and compensatory hypertrophy supervene. Strain leads to exhaustion and failure. He also expressed the belief that most cases of idiopathic hypertrophy are the result of the status lymphaticus and that only in exceptional instances do other factors act as causes. Bluehdorn (17 in the table) reported a case in which he, too, found round cell infiltration, degeneration of the muscles, and enlargement of the thymus, but in view of the fact that the patient suffered from eczema and fresh primary tuberculous infection of the lung, he said that these may have been the cause of the histologic appearance. On the basis of his case and the ones reported, Krstulovic (19 in the table) postulated a recurrent myocarditis, although his case presented only hypertrophy of the muscle fibers on histologic examination.

Howland (14 in the table), in discussing the literature and his five cases, in one of which there was a thymus weighing 22 Gm., pointed out the ignorance concerning the real limits of the size and weight of the normal thymus, and therefore that the diagnosis of idiopathic hypertrophy of the heart must not be precluded simply because of an apparently enlarged thymus. Furthermore large thymuses are not infrequently found when the cause of death is definitely ascertained; and enlargement of the thymus may be tremendous when abnormalities of the heart do not exist. He admitted, however, that when there is concomitant enlargement of other organs—the liver, spleen, and others—there may be reason to assume an association. He said that he could not conceive that any extra-uterine condition could lead to such an enormous enlargement, but he found it equally difficult to conceive of any intra-uterine condition of such a nature.

Five cases are reported by Oberndorffer (9 in the table), in two of which the patient had enlarged thymuses. In his report, he divided the so-called idiopathic hypertrophy of the heart into three varieties: (1) myocardial disease; (2) hypertrophy associated with hypertrophy of the thymus and status lymphaticus, and (3) pure idiopathic hypertrophy, the majority of cases of this type which he said are associated with some congenital lesion. Wiesel [5] expressed the belief that a hyposecretion of the chromaffin system leads to the sudden death. Hedinger

4. Ceelen: Klin. Wchnschr. **27**:27, 1916.

5. Wiesel: Virchows Arch. f. path. Anat. **176**:103, 1904.

(8 in the table), modified this idea and assumed that perhaps a hypersecretion leads to idiopathic hypertrophy. Michaud (12 in the table) said that the hyposecretion may lead to a fixation in dilatatoin because of the variation of the blood pressure, and that hypertrophy follows as a compensatory measure. Both Hedinger and Michaud admitted their lack of microscopic observations to substantiate their hypotheses. In the report of one of Hauser's (3 in the table) cases, he explained the enormous enlargement on the basis of an antecedent pertussis in which the attacks of coughing were as many as fifty a day, and after which the coughing persisted for five months. The plethora and stasis in the abdomen as well as the increased pressure in the lungs were sufficient, according to Hauser, to cause the enlargement. Michaud, Oberndorffer and Hochsinger [6] expressed the opinion that the cases reported in older children may have been congenital or dated back to earliest childhood.

CLINICAL CONSIDERATIONS AND COMMENT

Enlargement of the heart should be considered truly idiopathic only in the absence of organic disease, even if it is congenital or acquired, or in the absence of myocardial disease, such as described by Riesenfeld and Ceelen, Bluehdorn and in the present report. This reduces the number of true cases to seventeen. In these, as well as in the others recorded in the table, it is striking that there are so few clinical manifestations of the presence of such extensive involvement of the heart. Certainly the few symptoms and signs present are not commensurate with the pathologic changes. It is of interest, too, that the history is usually negative for any known antecedent illness which might have played an etiologic rôle. Most of the children are said to have been well previous to the terminal illness, which was usually of short duration. Death was sudden and as a rule unexpected. Enlargement of the heart was noted clinically in ten instances. Dyspnea, usually not marked, was not infrequently present, but it must be noted that in a few instances terminal bronchopneumonia was found. Cyanosis of varying degree was also frequently noted, but usually only immediately before death. Preterminal cramps, fainting spells, weakness, vomiting and anemia occasionally were reported in the histories, and these too were cited as occurring shortly before the demise of the patient. Systolic murmurs were heard in five of the cases of true idiopathic enlargement, and these were apparently functional since necropsy did not reveal any organic cause for them.

Howland said that he felt that it should not be impossible to make a clinical diagnosis of idiopathic enlargement of the heart; the history of

6. Michaud, Oberndorffer and Hochsinger: Beilage, Mitt. d. Gesellsch. f. inn. Med. u. Kinderh. in Wien. **40**:94, 1907.

attacks and the presence of dyspnea in the absence of evidence of pulmonary or congenital cardiac disease should be suggestive of its presence. It must be emphasized, however, that a history of attacks was infrequent in the majority of cases, and that other suggestive symptoms were absent until death. In eight of the truly idiopathic cases, actual hypertrophy of the muscle cells was reported on microscopic examination. In some, the hypertrophy or enlargement predominated in one chamber, in others in another; in a few it was generalized. The enlargement was not more frequent on either side of the heart. The average weight of the truly idiopathic hearts (weight of three of the seventeen not given) was 110.5 Gm. as compared to a normal weight of from 37 to 45 Gm. for the average age of 14 months. Many observers called attention to the fre-

Fig. 7.—Posterior and anterior surfaces of the heart of 15 months old infant, showing marked enlargement.

quency of death at the age when the infant encounters great strain in the attempt to walk and in other physical exertion; they believe it to be a contributory factor in the collapse. That an idiopathic hypertrophy may be congenital cannot be gainsaid, for a case of Simmonds and one of Oberndorffer occurred in new-born infants. Whether the others were also congenital is not definitely shown. It is, however, conceivable that a congenital condition of this nature may lie dormant until an infection or an added strain, such as walking, or violent and persistent coughing, as in pertussis, may initiate or precipitate a failure of the heart. In the case here reported, the cause of the infiltration and the degeneration in the musculature is not by any means clear. Antecedent history which might reveal a cause is absent. A histologic picture resembling the one here described is seen in many infectious diseases,

particularly in diphtheria, but also after carbon monoxide poisoning and in metabolic toxemia, such as uremia. It is noteworthy that in infancy and in childhood many toxic conditions exist which are occult and which might exert a deleterious effect on the heart. There was, then, in this instance a primary degeneration in the myocardium with accumulations of lymphocytes and a proliferation of the framework of connective tissue of the heart, the etiology of which is unknown. The gross appearance of marked enlargement (fig. 7) is explained on the basis of the generalized myocardial disease.

SUMMARY

1. By idiopathic enlargement of the heart is meant an enlargement of the entire organ or parts of it which cannot be explained on a pathologic basis either congenital or acquired. When myocardial infiltration or degeneration occur, the case cannot be considered as one of true idiopathic enlargement.

2. It is suggested that the term enlargement be used, since it is the most significant qualification which is at once clinical and anatomic.

3. A review of the literature of all cases considered or called idiopathic hypertrophy, enlargement, dilatation or congenital hypertrophy is presented and analyzed. Six of the total of thirty-four reported cases are excluded from consideration because of some anomaly or abnormality which might have played an etiologic rôle. In five of the remaining twenty-eight cases a histologic examination was not made. A thorough microscopic study is essential to establish the etiology and to classify the case. On histologic examination, six of the remaining twenty-three cases revealed myocardial disease which placed them outside the category of true idiopathic enlargement. There remain then only seventeen instances which might be considered true idiopathic enlargement of the heart in infancy and in childhood. It is conceivable that extensive histologic examinations might have revealed more frequently the presence of myocardial disease.

4. An additional case is presented which was considered idiopathic until microscopic studies of all parts of the heart revealed lymphocytic infiltrations and myocardial degeneration which was generalized enough to explain the enormous enlargement of the heart.

1085 Park Avenue.

AN UNUSUAL MECKEL'S DIVERTICULUM AS A CAUSE OF INTESTINAL HEMORRHAGE*

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The case of Meckel's diverticulum here reported is of interest on account of its unusual size and situation, and also because profuse intestinal hemorrhage was associated with it. Four other cases which resemble this one in regard to size and situation of the diverticulum have been located in hospital records and in the literature; also twenty-six cases of intestinal hemorrhage caused by Meckel's diverticulum have been found in the literature.

REPORT OF A CASE

History.—Merrill M., a boy, aged 11 months, was admitted to the Hospital for Sick Children, on Nov. 13, 1927, on account of refusal of food, constipation and loss of weight for three months. The patient was a full term infant, who had weighed 8¾ pounds (4 Kg.) at birth. The labor had been normal. He had been breast fed until 3 months of age, when he had been weaned on account of illness of the mother. A mixture of whole milk, water and sugar had then been given.

He had apparently developed normally until 5½ months of age, when he had had a profuse hemorrhage from the bowels. Five stools consisting largely of dark red blood, had been passed. According to the information obtained, the infant had been bright at this time, and no cause for the hemorrhage had been found. One month later, at the age of 6½ months, he had again passed two stools consisting largely of dark red blood. He had been taken to the local hospital and observed for one week. Again a cause for hemorrhage had not been discovered. Following his discharge from the hospital, he had gained weight. About three months ago, before death occurred, he had stopped gaining weight and had become constipated. A transfusion of blood had been given, apparently for its general tonic effect, but benefit had not been observed. The constipation had become more marked and the patient had refused the greater part of his feeding. The food had been changed to lactic acid milk, then "Mellin's Food," but improvement had not been noted.

Examination.—I first saw the patient three days before admission to the hospital. He was markedly emaciated, weighing only 10¼ pounds (4.6 Kg.). The chief point of interest was the presence in the upper right quadrant of the abdomen of a definite mass which projected out into the flank. Marked peristaltic waves were seen passing from the region of this mass across the abdomen from right to left. Smaller peristaltic waves were seen all over the abdomen. Immediate admission to hospital was advised, but the parents delayed this three days.

On admission to the hospital, the mass could not be felt in the abdomen, and peristaltic waves were not seen. The patient appeared to be a poorly nourished infant. The blood picture was normal. Pus cells or other abnormalities were not found in the urine. A guinea-pig was inoculated with the urine on

* Received for publication, July 2, 1928.

* From the Medical Wards of the Hospital for Sick Children.

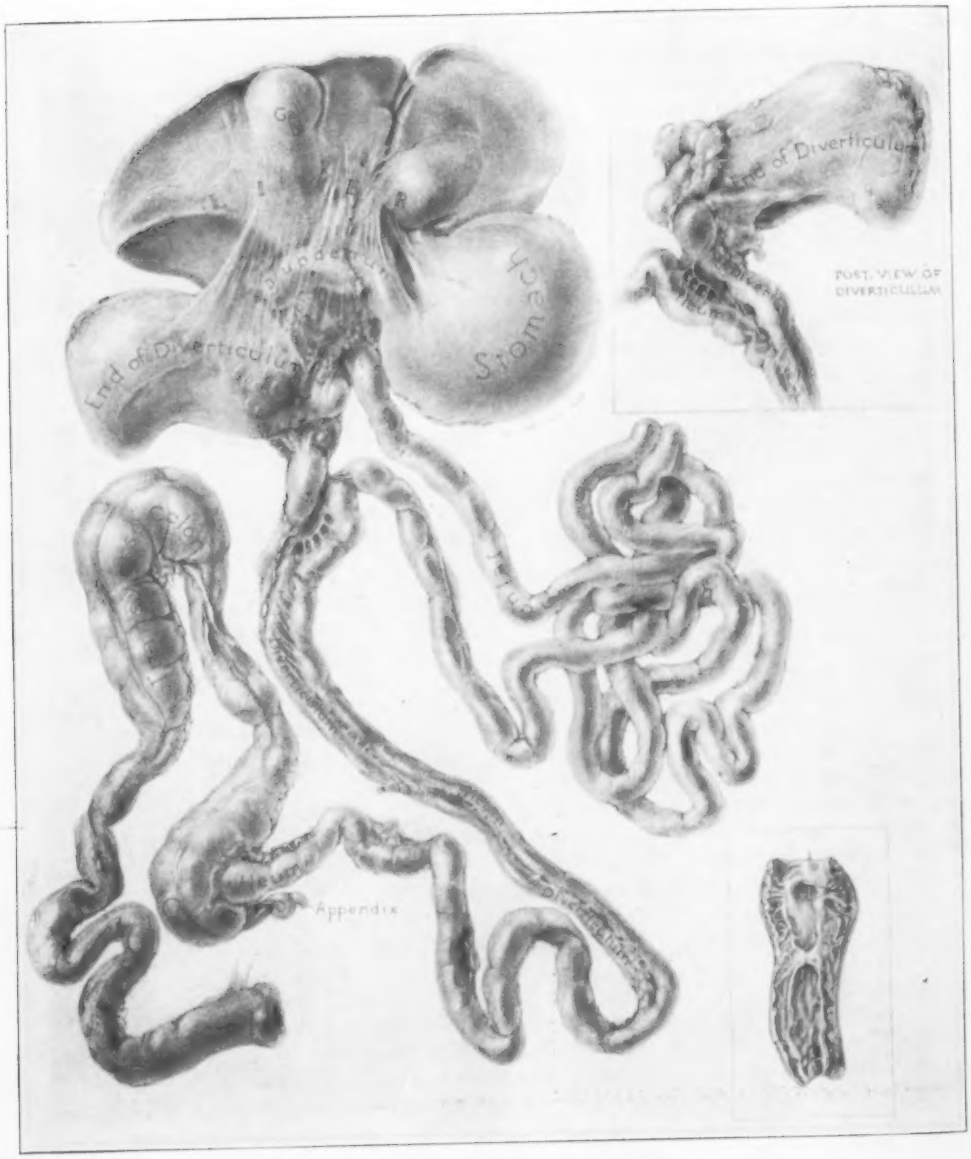
November 18. Subsequent examination of the pig did not show any evidence of tuberculosis. Repeated tuberculin tests were performed on the infant, with negative results.

The patient was placed on a diet of whole milk, farina and zweibach. He gained from 10½ to 12½ pounds (4.7 to 5.7 Kg.) in three weeks. The stools averaged from two to three a day and were normal. Vomiting did not occur. At this time, the abdomen became distended and constipation developed so that an enema had to be given daily. The stools were yellow, somewhat loose and occasionally mucus was present. Some peristaltic waves were seen, but a mass could not be felt. After this condition had persisted for three weeks, during which time the patient lost 1½ pounds (0.7 Kg.), the mass again appeared. It could be felt on the right side of the abdomen about the level of the umbilicus and extended up to the costal margin. Laterally, it produced a slight projection of the abdominal wall well out in the right flank. It was firm. Peristaltic waves started over the mass and passed across the abdomen from right to left. On the morning of December 31, the condition of the infant was the same as had been noted previously. When examined at 1 p. m., the mass had disappeared; however, there was a slight sense of resistance in the right upper quadrant suggesting the presence there of more fecal material than in the rest of the abdomen.

The infant's general condition then improved, and his weight increased over 2 pounds (0.9 Kg.) in two weeks. The abdomen, however, remained markedly distended. The increased resistance to pressure remained in the right upper quadrant of the abdomen, and at times the tumor could be readily palpated. On Jan. 12, 1928, the patient developed an infection of the upper respiratory tract, and died on January 14.

Autopsy.—The following is the report of the autopsy observations as made by Dr. I. H. Erb, hospital pathologist: When the abdomen was opened, the peritoneum was found to be smooth and glistening. There was no evidence of inflammation. The inner surface of the umbilicus was normal. Both the large and small intestines were markedly distended with gas. On removing some of the intestinal coils, a large mass was found lying retroperitoneally. It occupied the entire upper right quadrant of the abdomen extending laterally from the right flank to slightly beyond the midline and vertically from the lower posterior border of the liver to the sacral promontory. It was approximately the size of the stomach. Part of the cecum, the ascending colon and the proximal portion of the transverse colon lay over the mass.

On removal of the intestines, it was found that the lesser omentum stretched from the lower border of the liver to the upper surface of the tumor. The lateral free border of the omentum extended farther to the right than usual. On the upper surface of the tumor, the omentum divided into two layers, one reflected directly backward to the posterior wall of the abdomen and the other reflected anteriorly over the upper anterior surface of the tumor, then onto the anterior surface of the cecum and large bowel lying over the mass. In this way, both the tumor and the overlying bowel were retroperitoneal. From the posterior lower surface of the mass, a tube identical in appearance with the small intestine ran forward in the layers of the mesentery for a distance of about 9 cc. This tube then fused with the normal small intestine and continued beside it for 50 cm., ending in a small, knoblike enlargement of the small bowel 45 cm. from the cecum. Although fused with the normal bowel, the abnormal tube could readily be distinguished throughout its entire length. It is to be noted that the abnormal tube lay throughout its course in the layers of the mesentery and ended in the proximal or mesenteric side of the normal bowel.



Diverticulum with dilated end.

When the bowel was opened, it was found that the abnormal tube was in the nature of an outgrowth from the normal bowel. Throughout the fused portion a single wall separated it from the lumen of the normal bowel. Shortly before the abnormal tube entered the tumor, it was markedly constricted and fibrosed at two points, so that only a very small probe could be passed. The wall of the tumor was somewhat thicker than a wall of the stomach. The tumor was filled with clear fluid and some material resembling meconium. The remaining portion of the tube could not be distinguished macroscopically from the normal bowel. Evidence of an ulcer was not found.

Microscopic Examination.—Microscopic examination of the diverticulum showed the presence of the following tissue layers: an outer layer of loose connective tissue, a longitudinal muscle layer, a circular muscle layer, a connective tissue layer representing the submucosa, a smooth muscle layer representing the muscularis mucosae and then the epithelial lining. The wall between the fused portion of the diverticulum and the intestine was made up largely of loose connective tissue in the middle of which passed a few strands of circular muscle fibers. Each mucous membrane possessed its own muscularis mucosal. The striking feature of the mucous layer of the diverticulum was the presence throughout its whole course, including the tumor, of great numbers of gastric cells. Pancreatic tissue was not found in the diverticulum.

COMMENT

During the early weeks of fetal development, the midgut is connected to the vitelline vesicle by a fine tube, the vitelline duct. Normally, this tube atrophies and the bowel becomes completely separated from it leaving no trace of its attachment. The only remains of the duct normally found are occasional cells in the umbilical cord. In from 1 to 3 per cent of patients, however, this normal obliteration does not occur. The outer part in connection with the umbilicus may remain as a cordlike structure, while the proximal portion connected with the ileum remains patent and forms a diverticulum. This structure, the typical Meckel's diverticulum, is usually from 2 to 3 cm. in diameter and from 3 to 10 cm. in length. It projects from the lower part of the ileum within 1 meter of the ileocecal valve. The free end of the diverticulum may be connected to the umbilicus by the cordlike structure. This does not always occur, however, so in many cases the diverticulum hangs freely in the abdominal cavity.

The present diverticulum is unique on account of its unusual situation. It projected from the ileum about the customary distance from the ileocecal valve, but instead of coming from the distal or free side of the ileum, it arose from the proximal or mesenteric side. It then extended upward in the layers of the mesentery and fused with the normal bowel for a distance of 50 cm. The diverticulum then became free, and after two constrictions, ended in a large tumor about 10 cm. in diameter.

This tumor, or swelling, at the end of the diverticulun was no doubt caused by the constrictions shutting off the lumen with a resultant distention of the distal portion by the secretions.

In the records at the Hospital for Sick Children I have found a case of Meckel's diverticulum which originated from the mesenteric side of the ileum 8 inches (20.3 cm.) above the ileocecal valve. The diverticulum was 9 inches long (22.9 cm.) and during the first 3 inches (7.6 cm.) of its course, it lay between the layers of the mesentery. The remainder lay free in the abdominal cavity. One of the cases reported by Abt and Strauss,[1] consisted of a Meckel's diverticulum 18 inches (45.7 cm.) long which originated 4 inches (10.2 cm.) above the ileocecal valve and was so situated that it ran parallel to the ileum and enclosed in the mesentery. The wall of the diverticulum was constricted at three points. Moll[2] recently reported a giant Meckel's diverticulum which closely resembled that in my case. It arose from the antimesenteric wall of the ileum 2 feet (60.9 cm.) above the ileocecal valve. The diverticulum crossed over the ileum to become attached to its mesenteric border. It then fused with the gut and after extending upward for 3½ inches (3.7 cm.) terminated blindly. Another specimen resembling that in my case was recently presented to the museum of the Royal College of Surgeons by Arthur Edmunds. I am greatly indebted to Sir Arthur Keith for a detailed description of this specimen. It consisted of a diverticulum of the ileum which ran parallel to and fused with the intestine for 40 cm., lying on the mesenteric surface of the gut between the two layers of the mesentery. It then left the intestine and projected freely into the peritoneal cavity, this free portion being 25 cm. in length, completely enclosed in peritoneum and terminating in a rounded, blind extremity. These cases indicate that it is not an extreme rarity for a Meckel's diverticulum to lie between the layers of the mesentery or even to become fused with the intestine.

There is little doubt that intestinal hemorrhage associated with Meckel's diverticulum occurs more frequently than is usually supposed. Schaetz[3] discovered gastric epithelium in Meckel's diverticulum in five of thirty patients (16.6 per cent). Stulz and Woringer[4] found in the literature thirteen cases of peptic ulcer in Meckel's diverticulum. In eleven of these patients, there was associated intestinal hemorrhage. These authors also reported two cases of their own in which intestinal hemorrhage was a prominent symptom. Abt and Strauss[1] reported three cases of intestinal hemorrhage associated with Meckel's diverticulum. They also found in the literature three cases overlooked by Stulz and Woringer. During the discussion of the paper by Abt and

1. Abt, I. A., and Strauss, A. A.: Merkel's Diverticulum as Cause of Intestinal Hemorrhage, J. A. M. A. **87**:991 (Sept. 25) 1926.
2. Moll, H. H.: Brit. J. Surg. **14**:176, 1926.
3. Schaetz, G.: Beitr. z. path. Anat. u. z. allg. Pathol., 1925, vol. 74.
4. Stulz, E., and Woringer, P.: Ann. Surg. **83**:470, 1926.

Strauss, Moore added two cases and Stone one case. Other instances have been recorded by Mayo and Johnson,[5] A. S. Jackson,[6] McCalla [7] and Moll.[2]

The clinical history is singularly constant. In only one of these twenty-six cases was the patient a female. Intestinal hemorrhage and indefinite abdominal pain were the two outstanding symptoms. The earliest age at which the intestinal hemorrhage was first observed was 4 months. Frequently, there was only one profuse hemorrhage followed by apparent recovery for a period of months or years. Hemorrhage then recurred. Occasionally, there were repeated small hemorrhages. The patients usually showed little evidence of shock. No assistance in making a diagnosis was obtained by x-ray or other examination. The diagnosis was made only by means of an exploratory laparotomy or at autopsy.

CONCLUSION

An unusual case of Meckel's diverticulum has been reported. Intestinal hemorrhage was associated with it. The presence of a bleeding Meckel's diverticulum should be considered as an etiologic factor in cases of intestinal hemorrhage of obscure origin, particularly in male children.

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5. Mayo, W. J., and Johnson, A. C.: S. Clin. N. Amer. **6**:1127 (Oct.) 1926.
6. Jackson, A. S.: Ann. Surg. **85**:252, 1927.
7. McCalla, A. I.: Canad. M. A. J. **17**:79, 1927.

DILATATION OF THE DUODENUM

OR CHRONIC OBSTRUCTION OF THE DUODENUM CONGENITAL IN ORIGIN *

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AND
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OMAHA

During the last few years a number of articles have appeared on the dilated duodenum of the adult, and this condition is now recognized as a definite clinical entity. The symptoms, signs and x-ray appearance give a rather definite picture. In the adult, the condition is usually the result of some embryonic band, malformation, adhesions or compression by mesenteric root and artery. Although the subject of dilated duodenum has not been touched on by the pediatrician, there is no physical reason why the same picture might not occur in the infant and child. The case which will be reported here is one of constriction of the duodenum due to malformation and compression by the root of the mesentery. The history is typical of that of a dilated duodenum in the adult, and reemphasizes a more careful study of persistent vomiting in infancy and childhood and further dependence on the x-ray in difficult cases.

REPORT OF CASE

N., aged 6 months, brought to the office on Aug. 21, 1926, presented the following history: The father, aged 38, was well; the mother, aged 28, was well. There was one other child, aged 6 years. The mother had had one miscarriage. During pregnancy she vomited almost continuously, and was extremely nervous and fainted a number of times. The delivery was normal, and the child was born on Feb. 20, 1926. It weighed 8 pounds and 1 ounce (3.6 Kg.). The infant was bottle fed with Eagle Brand and modified cow's milk. It vomited from birth; at first this appeared to be persistent, occurring about every two weeks and lasting for two or three days; then the periods became shorter and vomiting occurred every third or fourth day. At the age of 5 months, the infant weighed 11 pounds (5 Kg.). It had a persistent attack of vomiting. On July 4, 1926, the infant was sent to the hospital under the care of the family physician, who diagnosed the case as pyloric stenosis and advised operation following a roentgenologic examination. The parents refused to allow an operation. On August 21, the infant weighed 13 pounds and 9 ounces (6.1 Kg.). There was a history of loose stools and profuse perspiration without fever. The infant was placed on a diet appropriate for its age consisting of modified cow's milk and cod liver oil. Seven days later there was no vomiting. The child weighed 14 pounds and 6 ounces (6.6 Kg.). On October 2, it weighed 17 pounds (7.7 Kg.). Eleven days later, on October 13, it had a vomiting spell and lost 9 ounces (0.2 Kg.). Thick gruel was given at this time. A month later, on November 13, the child weighed 17 pounds and 15 ounces (8.2 Kg.).

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* From the Department of Pediatrics and the Department of Anatomy, Medical Department of the University of Nebraska.

The bowel movements were good and the appetite was good. The infant was doing well. On December 11, it weighed 19¼ pounds (8.7 Kg.). Its condition was good, and there was no vomiting. On February 10, the infant was again seen at the office; it weighed 21 pounds (9.5 Kg.), the normal weight for its age.

On Sept. 23, 1927, the child began to vomit. At first, it seemed to have nausea and emesis of food followed by the forcible vomiting of green fluid. The stools

Fig. 1.—Dilated duodenum in the case reported. *Py.* indicates pylorus; *Du.*, duodenum; *T.C.*, transverse colon; *Om.*, omentum; *D.J.*, duodenojejunal junction; *Je.*, jejunum; *S. M. A.*, superior mesenteric artery; *M.R.*, mesenteric root. Normally, the transverse colon crosses the duodenum at point *A* and the duodenojejunal junction is at, or just above, point *B*.

were loose for a week preceding this attack. The urine was scanty. The child was restless, but cried little. Apparently, it did not have any pain. There was a slight elevation of the temperature. A strong acetone odor was noted on the breath. The urine contained a few pus cells, acetone and diacetic acid. There

was a marked loss of weight. The child was sent to the Methodist Hospital. A nasal gavage of soda solution and a lavage of dextrose, 10 per cent, and orange juice was given. Two hundred cubic centimeters of 5 per cent dextrose and saline were given intraperitoneally. The vomiting ceased, and the child was given protein milk by gavage every four hours and then fluids between feedings. It remained in the hospital four days. At the end of the fourth day, the child was eating vegetable soup, vegetables, cereals and diluted milk. The stools were large, soft and yellow. From this time on, the infant made a rapid recovery and gained in weight, and when it was seen at the office on November 10, it weighed 24 pounds

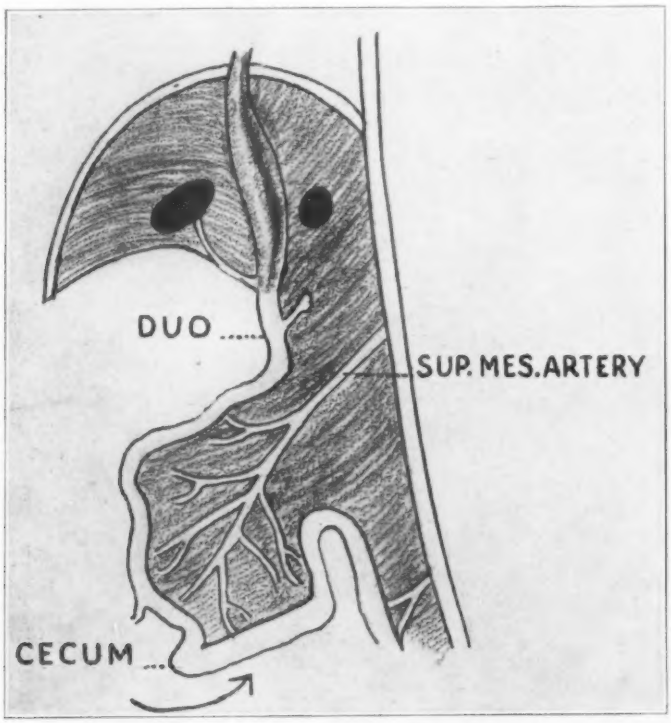

Fig. 2.—Rotation of intestine on the axis of the superior mesenteric artery. Arrow gives direction of rotation. *Duo* indicates duodenum.

(10.9 Kg.). When it was discharged from the hospital, it weighed 19 pounds (8.6 Kg.).

The infant vomited on Nov. 14, 1927. Ordinary means used by the mother seemed to control the vomiting. This occurred again on November 15, but on November 16, the vomiting persisted. One of us (J. A. H.) was called to the home in the evening. Examination disclosed a marked loss in weight, acidosis, nausea and vomiting of a greenish and yellowish fluid. The kidneys had not acted for eight hours, and showed all the evidence of a severe dehydration and acid intoxication. There was no pathologic change in the chest or head; the abdomen was flat, and a bowel movement had not occurred for twenty-four hours. The infant was sent directly to the hospital. Lavage of the stomach with soda solution was performed, and a feeding of protein milk was given; this was

retained until the next feeding. When the tube was passed four hours later, most of the feeding returned through it. During the night, the child was fed by lavage, but he did not retain much of the feeding. The following morning, the child weighed 19 pounds and 1 ounce (8.6 Kg.), a loss of 4½ pounds (2 Kg.) in four days. Dextrose was administered intraperitoneally, and two hours later, lavage of the stomach was performed. Soda solution and protein milk were administered, but shortly after the infant's temperature rose to 104 F., the extremities were cold, and the pulse rate was 218. The child was given stimulation and was conscious during this time; it would call for water. It died at 2 p. m. During this last period, one of us (J. A. H.) saw the infant at 8 p. m. the day before the infant died.

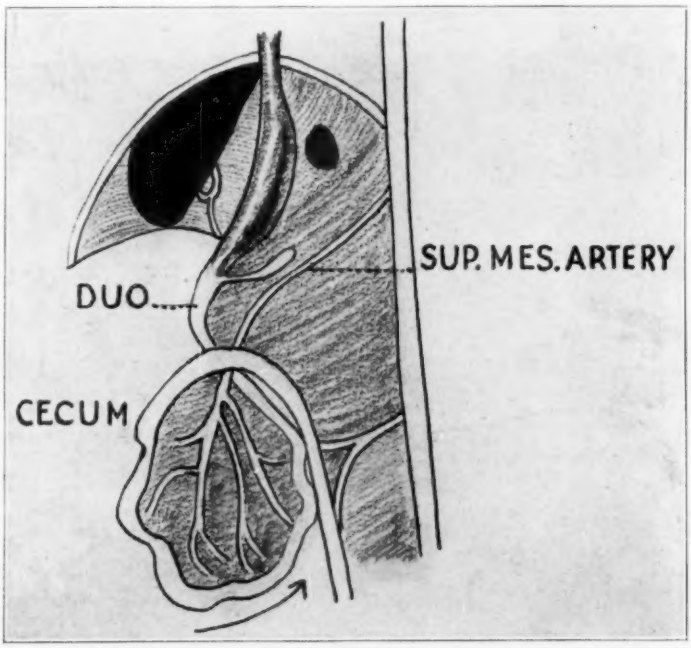

Fig. 3.—Intestine partly rotated on its axis. Superior mesenteric artery now crosses the duodenojejunal angle. *Duo* indicates duodenum.

COMMENT

The diagnosis in both attacks in September and November was acidosis or acid intoxication due to absorption from the intestinal tract, the result of a mechanical obstruction located in the small intestine.

Autopsy was performed by Dr. W. B. Moody, pathologist at the Methodist Hospital. When the abdomen was opened, a congenital malformation or arrested development of the intestinal tract was found; the cecum and appendix lay in the midline just behind the umbilicus, and the large intestine was not anchored. The entire intestinal tract

was removed, and the specimen was sent to Dr. C. W. M. Poynter and Dr. R. R. Best, anatomists of Nebraska University, for study. The accompanying illustrations and explanation illustrate the condition that was present at the time. Dr. Best's comments were as follows:

Chronic obstruction of the duodenum is a definite entity, yet many times it is not recognized. Usually, the obstruction is due to some embryonic band, malformation, adhesion or compression by the root of mesentery and superior mesenteric artery. This case belongs to a less

Fig. 4.—Dilated duodenum and retention of the barium.

frequent cause, the incomplete rotation of the intestine on its mesenteric axis. Normally, the intestine rotates 270 degrees on this axis in the counter-clockwise direction. This brings the primitive cecum into the right upper quadrant beneath the liver, from which position it descends by growth. If this intestine had rotated completely, instead of only about 160 degrees, the colon would have crossed the duodenum at point *A* (fig. 1) and the duodenojejunal angle would have been at or just above point *B*. Normally, the duodenojejunal angle is just to the left and on the same level as the mesenteric root. Here, it was yet to the right of the mesenteric root. There was definite partial obstruction at

the duodenojejunal angle, caused not only by the twisting and fixation of the jejunum on its longitudinal axis between the duodenojejunal flexure and point *B*, but also by the dragging of the transverse colon. The mesenteric root was also compressing the jejunum. Naturally, the loaded ascending and transverse colon increased the obstruction more than the empty colon, and permitted intermittent attacks of duodenal toxicosis, which resulted in vomiting and dehydration.

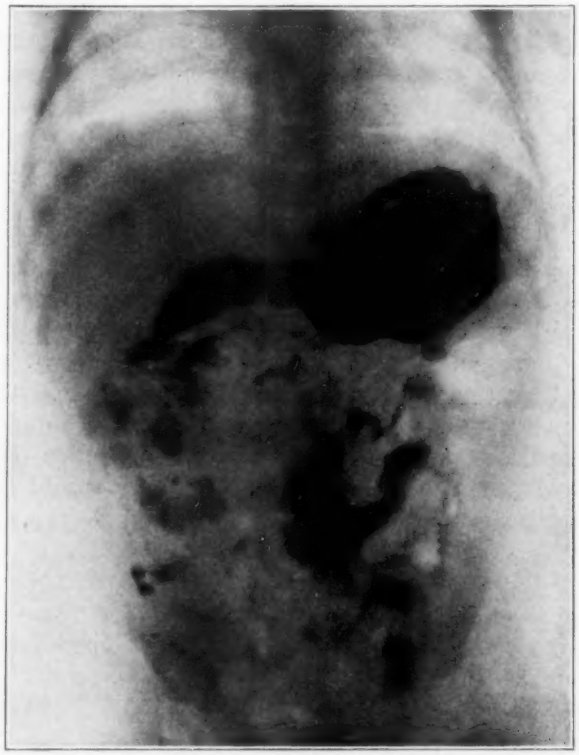

Fig. 5.—Three hour residual, showing the retention in the stomach and dilatation of the duodenum.

It is my belief that this patient could have been helped surgically by raising the hepatic flexure and transfixing it to the lateral abdominal wall. The constriction by the root of the mesentery was most marked at its left border near point *B* (fig. 1); a small transverse incision sewed up longitudinally would have released this to some extent. Fortunately, the superior mesenteric artery ran along the right border of the mesenteric root. A supramesocolic duodenojejunostomy would possibly have benefited the case, although there would have been an extremely long loop.

Following the death of the infant, the x-ray picture was obtained from the physicians who were in charge of the case the first few months of the child's life. These were taken on July 4, at the age of 5 months. A diagnosis of pyloric stenosis or obstruction was made on account of the retention of barium in the stomach three hours after the administration of a barium meal. These x-ray pictures were given to Dr. Pierce, the roentgenologist of the Methodist Hospital, for diagnosis. On examining them, Dr. Pierce immediately recognized a markedly dilated duodenum and pointed out the difference of the contour of the stomach and duodenum; and the accompanying figure 4, taken immediately after the administration of the barium meal, shows the markedly dilated duodenum. Figure 5, taken three hours later, shows a large residue in the stomach as well as in the duodenum. These x-ray pictures were taken by competent men, but unfortunately the condition was overlooked at the time.

CONCLUSIONS

Following the first examination, the infant made a rapid gain in weight, and then apparently overcame the obstruction. At the age of 1 year, the child was normal in weight and was not again observed until the attack some months later. A diagnosis of the underlying condition could have been made with extensive laboratory study. The history, postmortem observations, proper interpretation of the x-ray plates and knowledge gained through the postmortem examination, give a good description of this condition which in the future should be of great assistance in making a diagnosis.

ACUTE TORSION OF AN UNDESCENDED TESTIS IN AN INFANT, AGED EIGHT MONTHS*

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PITTSBURGH

Acute torsion of the testis in its proper position in the scrotum is fairly common, even in new-born infants. Taylor [1] reported a case of congenital torsion of the right testis in the scrotum in a new-born infant who was operated on at the age of 2 days. Beggs [2] recorded the case of an infant who was operated on at the eleventh day, and Nash [3] recorded one which occurred at the fifth day, and the infant was operated on at the ninth day. Many other similar cases have been reported.

Acute torsion of the undescended testis in the inguinal canal is, however, a rare occurrence. In 1913, Farr [4] could find only four cases of torsion of an undescended testis in infants, under 1 year of age, reported in the literature up to that date. He reported one case of his own in an infant aged 7 months, with torsion in the left inguinal canal. Dowden [5] reported a case which occurred at 5 months of age; Lofberg [6] recorded one at 3 months and another at 9 months, all three cases being left-sided. Day [7] reported a right-sided case in an infant, aged 6 months; Mixter [8] mentioned a case in an infant, aged 8 months, who required orchidectomy, but he did not mention the side affected. Thorek,[9] in a summary of cases resembling strangulated hernias, quoted a case of Phocas',[10] in an infant, the age and affected side of which were not mentioned.

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* Received for publication, June 28, 1928.

* From the Pediatric Service, Montefiore Hospital.

1. Taylor, M. R.: A Case of Testicle Strangulated at Birth, Brit. M. J. **1**:458, 1897.

2. Beggs, R. C.: Torsion of the Testis Occurring During or Immediately After Birth, Brit. M. J. **2**:843, 1921.

3. Nash, W. G.: Torsion of the Testicle in an Infant, Brit. M. J. **1**:267, 1921.

4. Farr, Charles: Strangulation of the Undescended Testis, Ann. Surg. **58**: 838 (Dec.) 1913.

5. Dowden, Scot: M. & S. J., 1901, p. 221.

6. Lofberg: Hygeia **73**:1081, 1911.

7. Day, H. F.: Torsion of an Undescended Testicle, Ann. Surg. **38**:277 (Nov.) 1924.

8. Mixter, C. D.: Undescended Testicle, Surg. Gynec. Obst. **39**:275 (July) 1924.

9. Thorek, Max: Torsion of Spermatic Cord with Undescended Testicle Simulating Strangulated Hernia, Interstate M. J. **26**:194 (March) 1919.

10. Phocas: Ann. de mal de org. genito-urin. **22**:454, 1904.

Normally, the testis descends into the scrotum at from the eighth to the ninth month of fetal life, but in Holt's [11] experience, in 10 per cent of male infants at birth, one or both of the testes were not in the scrotum. In most infants, descent occurs without difficulty in the first weeks of life and does not cause any symptoms. But, as Morse [12] said, it must not be forgotten that in infants and young children the testis easily slips back into the inguinal canal; the diagnosis of undescended testis therefore is not justified unless the testis is constantly absent from the scrotum or constantly in the inguinal canal. The completion of the descent of the testis usually occurs in the first weeks of life, or at least in the first year, but may be accomplished as late as from the ninth to the eleventh year, or even as late as the twenty-second year.

Lucas [13] stated that the testis may be arrested at any part in its descent from the kidney to the scrotum. To understand the problem of incomplete or anomalous descent of the testis, one must consider the mechanism by which it reaches the normal position. In early fetal life the testis lies high on the posterior abdominal wall. At its lower pole is attached the gubernaculum, which has been compared by Eisendrath to a four-tailed ribbon, the strongest part being attached to the scrotum and the other three tails attached respectively to the inguinal region, the perineum and the pubes. The actual descent is effected by the relative shortening of the gubernaculum. In reality, the body of the infant grows faster than the gubernaculum so that the testis is gradually pulled down into the scrotum. Any factor that interferes with the rate of growth will cause incomplete descent of the testis, and any factor that promotes the pull of the gubernaculum toward the other attachments will cause the testis to take up an abnormal position. As the testis reaches the scrotum, it pushes before it a process of the parietal peritoneum, which later becomes the tunica vaginalis testis. At birth, the canal between the abdominal cavity and the scrotum is wide and the testis can be easily pushed up into the abdomen. When the testis is undescended, it is usually pathologic and shows a decrease in the spermatogenic cells and an increase in the interstitial tissue. The scrotal sac is empty and hernia may occur. Other malformations or developmental defects often coexist. The undescended testis in its abnormal position is liable to injury and tends to atrophy. Malignant degeneration may occur. Inflammation

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11. Holt, L. E.: Diseases of Infants and Children, ed. 8, New York, D. Appleton & Co., 1922, p. 627.

12. Morse, J. L.: Clinical Pediatrics, ed. 1, Philadelphia, W. B. Saunders Company, 1926, p. 45.

13. Lucas, W. P.: Modern Practice of Pediatrics, ed. 1, New York, The Macmillan Company, 1927, pp. 49, 76.

is common; adhesions may result as in the case here reported. Gangrene may follow a torsion, the latter occurring more frequently on the left side.

Murray [14] believed that in every case of torsion of the testis there has been some degree of torsion from birth, and that torsion of the testis is of congenital origin and is not acquired. He believed that a constant feature of imperfect descent of the testis is a separation of the body of the organ from the epididymis by a long mesorchium, which allows some degree of rotation during the gubernacular slide. The suggestion, however, that torsion of the testis occurs in an undescended testis because of its free mobility is hardly tenable, since the mobility of the testis in the inguinal canal is not to be compared with that of the organ in the scrotum, which is frequently drawn up into the inguinal canal from the bottom of the scrotum.

Rigby and Howard [15] stated that if torsion of the testis is to occur, the testis must be attached to the spermatic cord in some unusual way. In their opinion, the congenital abnormalities present in all cases, whether the testis is fully descended or not, are: (*a*) the abnormal attachment of the common mesentery and vessels to the lower pole of the body and the globus minor so that the testis is attached by a narrow stalk instead of by a broad band; (*b*) elongation of the globus minor, and (*c*) the capacious condition of the tunica vaginalis.

The exact cause of the condition is, therefore, a matter of dispute. Small rings, a short cord, peritoneal adhesions, a loss of power or anomalous attachments of the gubernaculum; anomalous development of the generative tract in fetal life; reversion to a lower mammalian type and, according to Eisendrath, a deficiency in the development of the arching fibers of the internal oblique muscle with a weak conjoined tendon, have been variously given as causes.

Uffreduzzi,[16] of Carles' clinic in Turin, believed that the condition is merely a local expression of infantilism, i.e., of a serious retardation of the development of the whole individual and is nearly always accompanied by other bodily or mental abnormalities. Coley,[17] quoting Uffreduzzi's work, said that he had found marked signs of physical or mental abnormalities associated only with double undescended testes, never in unilateral cases.

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14. Murray, R. W.: The Etiology of Torsion of the Testicle, Brit. M. J. **2**: 7, 1912.

15. Rigby, H. M., and Howard, R. J.: Torsion of the Testis, Lancet **1**:1415 (May 25) 1907.

16. Uffreduzzi, O.: Contributo sperimentale alls conoscenza del testiolo ritenuto, Gior. d. r. Accad. de med. di Torino **16**:36, 1910.

17. Coley, W. B.: Operative Treatment of Undescended or Maldescended Testis, Surg. Gynec. Obst. **28**:452 (May) 1919.

SYMPTOMS AND PHYSICAL SIGNS

Usually, there is severe pain in the groin, but as in the case presented, there may be an apparent absence of much pain or tenderness. Vomiting is usually an early symptom, but is not a constant feature. The bowels react to enemas and purgatives, and gas is passed. In some cases, general constitutional symptoms are almost absent. Frequency of micturition has been reported. The temperature is usually normal or only slightly elevated. Examination shows a swelling in the groin the size of a hen's egg, but is sometimes larger, usually placed obliquely above Poupart's ligament in the site of the inguinal canal. If the condition is of some duration, there will be found marked redness, swelling and edema of the tissues along the inguinal canal extending into the scrotum on the same side. The infant holds the leg drawn upward, on the affected side. The testis is absent from the corresponding side. Impulse is not found on coughing, and increase of size is not found on crying. The tumor is irreducible.

DIAGNOSIS

There may be difficulty in distinguishing a testis in the inguinal canal from an enlarged gland in the same location, as both are solid. The suddeness of onset in torsion, the absence of the testis from the scrotum on that side, the absence of any etiologic factor for an enlarged gland is in favor of the tumor being a testis.

The diagnosis from strangulated hernia is more difficult, and indeed strangulated hernia may be a complication. The absence of the testis from the affected side, the ovoid shape of the testis and its solidity may aid, but the swelling in both cases may be similar and the local signs may be deceptive. In torsion, the general symptoms are not so severe and the patient is not so shocked; there is not such persistent vomiting and it is never fecal; the bowels react to enemas and purgatives; gas is passed, and abdominal distention is not present.

In infants the question of diagnosis from acute epididymoorchitis, syphilis and tuberculosis, especially in the undescended cases, will rarely arise.

REPORT OF CASE

CASE.—J. M., a boy, white, aged 8 months, was born at full term with a normal delivery and was breast fed until 6 months of age, since then he had been fed from the bottle. The family history was negative for undescended testis. The previous history did not reveal any serious illnesses, but the infant had always been cross, fretful, subject to attacks of gas and colic and had never slept well at night. The bowels were usually constipated; urinary difficulty had not existed. There had been an occasional spitting up after he had been fed with the bottle, but he had not vomited.

The mother said that she had not noted a mass in the groin until the evening before the infant was taken for examination, and believed that the mass appeared suddenly in the left inguinal region after a severe crying spell.

A physical examination on Nov. 17, 1927, showed a fairly well nourished, pale, male infant, with little evidence of shock or distress. He weighed 17 pounds, 2 ounces (8 Kg.). The results of the physical examination were negative except for the finding of an ovoid mass in the left inguinal canal, 3.5 cm. long, which was practically immovable and irreducible. When the child was crying, impulse was not felt on straining, and there was dulness to percussion. The tissues over the left inguinal canal and extending into the scrotum were reddened, swollen and edematous. The left scrotal sac was much swollen but did not contain a testis. The right testis was in the normal position in the right scrotum. The abdomen was not distended, and pain, rigidity and tenderness were not felt on palpation. The results of the rectal examination were negative. The temperature was 99.5 F. and the blood count and the urine were normal.

An operation was performed on November 17, by Dr. J. M. Jackson, who used and ether anesthesia. An incision was made over the tumor in the left inguinal canal parallel to Pourpart's ligament. The tissues were markedly swollen and reddened. The tumor was exposed by blunt dissection and was found to be surrounded by rather dense adhesions. The spermatic cord was twisted twice to the right and the testis was blackish and appeared gangrenous. Untwisting of the cord and the application of heat failed to restore the circulation. The cord, which was extremely short, was ligated high up near the internal ring and the stump was sutured to the under surface of the conjoined tendon, and the latter was again sutured to the aponeurosis to prevent a subsequent hernia. The wound was closed in the usual manner. An uneventful recovery occurred.

The pathologic report was made by Dr. K. Yardumian. The specimen was a testis, markedly discolored and edematous. The tunica striped off easily on account of a considerable amount of hemorrhagic fluid between the layers. The testis proper was blackish and appeared gangrenous. The epididymis was distended and showed necrotic changes. Microscopic examination showed the stroma studded with large hemorrhages; the vessels were dilated. The seminiferous tubules were much distorted and irregular in outline because of the hemorrhagic contents. The epithelial lining of the tubules was extremely granular, and the nuclei were faded. There was a cloudy swelling of these cells. The lumen of the tubules was filled with lymphocytes and red blood cells. There were areas of focal necrosis. The whole picture was that of gangrene, which resulted from obstruction of the circulation of the testis.

TREATMENT

The preventative treatment is the replacement into the scrotum, when possible, of the undescended testis in the inguinal canal, by repeated daily traction. A truss with a soft pad may be applied to prevent its return into the canal. If it cannot be brought down into the scrotum by the sixth year, operation is advisable. Some physicians advise waiting until puberty for operation in order to give the testis a chance to descend during the growing period.

When torsion has occurred, an attempt may be made, if the case is seen early, to turn the testis in the canal before operation, or even to bring it down into the scrotum. This is rarely successful. Operation is usually indicated as soon as possible; if done early it may be possible to save the testis by untwisting the cord and by stitching the testis in position in the scrotum, although sloughing, gangrene or atrophy may

result. When the cord is too short, the vessels are usually of insufficient length to allow for any lengthening of the cord by traction; here Bevan's [18] operation may be performed, in which the vessels are divided without other injury than marked atrophy of the testis. The vas will usually be found long enough to permit of transplantation of the testis; a certain amount of stretching does not incur any risk.

While the gland should never be needlessly sacrificed since the internal secretion is still present, although it may be useless as far as reproduction is concerned, when gangrene is already present and when heat fails to cause a return of the circulation, removal is indicated. Max Thorek [9] stated that it is plainly evident from a study of the literature that in twisted spermatic cords, particularly when they are ectopic with short mesorchium and with clear evidence of a beginning degeneration of the testis involved, that castration seems the only rational method of procedure. The risks of sloughing, septicemia and peritonitis if it is not removed and the rapid recovery following removal leaves little in favor of trying to allow such testes to remain. Replacement into the abdominal cavity is not advisable, as there is danger of degeneration or later malignancy.

SUMMARY

A case of torsion of an undescended testis in the left inguinal canal is reported in an infant, aged 8 months. This is a rare case in surgical pediatrics.

A resumé of the etiologic factors and the theories of causation of the condition is presented, together with a discussion of the symptoms, physical signs, diagnosis and treatment.

18. Bevan, A. D.: Undescended Testicle, Surg. Clin., Chicago **2**:1101 (Dec.) 1918.

CORRECTION

An error occurred in the legend appearing under figure 5, in the article by Dr. Alfred E. Fischer on "Fetal Peritonitis" in the last issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN (**36**:774, 1928). The legend should read: Note that the outer wall of the intestine is formed only by longitudinal muscle.

Progress in Pediatrics

IMPROVING THE VALUE OF THE INFANT MORTALITY RATE AS AN INDEX OF PUBLIC HEALTH EFFORT *

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Since 1915, when the United States Census Bureau designated the birth registration area, making available accurate figures on infant mortality, a stratification of the infant mortality rates of the cities of this country has been apparent annually. The high infant mortality rates of southern cities, the low rates of the Pacific coast cities and the rates of the cities of the middle Atlantic states, occupying an intermediate position, are phenomena well known to all observers of this important health index.

Infant mortality rates have declined annually since 1915, but the decline has not altered the manner of variation. In 1915, in a group of five cities, including Richmond, Buffalo, New Haven, St. Paul and Seattle, the infant mortality rates were arranged in that order, Richmond having the highest rate and Seattle, the lowest. In 1927, the infant mortality rates of all of these cities had declined markedly, but the order remained the same, Richmond still having the highest rate and Seattle, the lowest.

In three years of this thirteen year period, there was an interchange in the position of two cities; for ten years, however, the infant mortality rates of these five cities, representing different geographic areas, have maintained a characteristic relation toward each other.

CORRECTION OF RATES FOR "EXTERNAL INFLUENCES"

The constancy of this variation makes apparent the unfairness of comparisons of "uncorrected" infant mortality rates as indexes of the success or failure of public health work. If the rate of Seattle is low because an equable climate protects its infants from extreme heat in summer and from excessive cold in winter, then the minimum infant mortality rate attainable by this city, other health conditions being optimum, will be lower than that of a city having unfavorable weather

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conditions. A forecast of the "minimum" infant mortality rate of a city determined by its local or sectional characteristics may be used as a base from which to measure more fairly the efficiency of public health work. The amount by which the actual infant mortality rate is lower than the "minimum" predicted may be the result of a factor affecting infant mortality favorably in this city, although of negligible effect in the majority of cities, and therefore not included among the factors used to forecast the "minimum" rate. If the relation of such factors is studied and the necessary correction made, then the remainder of the reduction over the "minimum" infant mortality rate may be taken as an indication of the favorable effect of the general public health program, and particularly, of infant hygiene work. An excess of the actual over the predicted "minimum" infant mortality rate similarly demands search for additional local factors which may affect infant mortality unfavorably; the correction for these being made, the excess remaining indicates the further reduction which public health effort is free to bring out.

TABLE 1.—*Variation in Urban Infant Mortality Rates in Five Cities of the United States from 1915 to 1927*

City	Infant Deaths per 1,000 Live Births in			
	1915	1920	1925	1927
Richmond	127	114	91	80
Buffalo	108	103	86	71
New Haven	87	87	66	54
St. Paul	78	73	58	49
Seattle	53	57	45	41

Numerous studies have shown the importance of order of birth, sex, health of the mother, method of feeding (breast vs. artificial), etc., as causative factors in infant mortality. These factors, indisputably important, may be classified, however, as "internal," to be distinguished from certain "external" factors such as climate, color and nativity of the population, and its educational, economic and occupational status. "Internal" and "external" factors are evidently closely associated, and variations of the latter have significance because of the more fundamental variations of the former which they reflect.

The collection of data of the first class is possible only through study of individual cases, requiring an extensive field investigation; data on the group of external factors, climatic conditions, demography, economic, occupational and educational status, on the other hand, are readily available in reports of the various federal bureaus. The resources available for this study did not permit field research, and it was therefore necessary to limit the investigation to a determination of the "external" factors having the greatest importance in forecasting minimum infant mortality rates.

What, then, are the factors of possible external influence on the infant mortality rate, classified under these broad headings? The demographic factors are birth rate (crude and refined rates), the color and nativity of the population, including under the latter the specific distribution of the foreign-born white persons according to country of birth. Educational status may be measured by the literacy of the population, economic and occupational status by the number of unskilled male workers and by the number of married women gainfully occupied. The climatic factors of theoretical importance are temperature of specific winter and summer months, sunlight and rainfall.

Certain interrelations of these factors are evident for cities grouped geographically. The cities of the south, for example, are characterized by the existence of a high percentage of colored population; they are also in the zone in which the temperature of the summer months is high. Furthermore, the number of colored women gainfully occupied in the cities of the south, is large. The relation of these factors to infant mortality rates and to each other, must, therefore, be determined quantitatively, the factors showing interrelations eliminated and only those factors retained which in themselves show a significant relation to infant mortality rates.

"EXTERNAL INFLUENCES" STUDIED BY CORRELATION METHOD

The correlation method offers a technic for such an evaluation of factors as is proposed. The determination of the coefficients of correlation between infant mortality rates and the various factors listed makes possible a preliminary selection of the most significant factors. The study of the coefficients of correlation between the factors themselves gives a basis for elimination of overlapping factors. The method of multiple correlation offers a means of determining the group of factors which, taken "in multiple," shows the highest correlation with the infant mortality rates of the cities studied. Finally, an equation showing the regression of infant mortality on this group of factors may be used to predict infant mortality rates, which will show agreement with the actual infant mortality rates equal to that indicated by the coefficient of multiple correlation.

SOURCE OF DATA

The infant mortality rates in a group of ninety-three apparently normal [1] cities having a population of 40,000 or more according to the census of 1920, and in the birth registration area during all or part of the period from 1921 to 1925, were selected for this study. The number

1. Cities showing an abnormal increase in population between 1910 and 1920, and those containing institutions for the care of children (especially designated by the U. S. Bureau of the Census) were omitted.

of cities was limited to ninety-three, since this was the maximum number for which complete data on temperature and rainfall could be obtained. When it was possible, the infant mortality rates and the factors correlated with them were used as averages for the period from 1921 to 1925. The data obtained from the Census of 1920, those on demography, educational, economic and occupational status, were necessarily of that year. Figures on "per capita effective income," from National Markets and National Advertising, Research Department, Crowell Publishing Company, were for 1926; data on income tax, from the reports of the Income Tax Unit, United States Department of the Treasury, were for 1925. The reports of the United States Weather Bureau were available annually, and the data on climate were therefore used as averages for the period from 1921 to 1925.

RESULTS OF SIMPLE AND MULTIPLE CORRELATIONS

A large number of preliminary correlations were made for the purpose of selecting factors which showed the highest correlation with infant mortality rates. The correlation between the percentage of colored people in the population of these ninety-three cities and their average infant mortality rates from 1921 to 1925 was relatively high, confirming the indications of infant mortality rates observed for white and colored populations. The correlation between infant mortality rates and the percentage of foreign-born white people was extremely low; when the foreign-born white population was studied according to its specific country of origin, however, some interesting correlations were revealed. The negative coefficient of correlation between infant mortality rates and the percentage of the population of Scandinavian birth was large enough to indicate definitely the association of low infant mortality rates with a high percentage of Scandinavians in the population. A slight tendency for low infant mortality rates to be associated with a high percentage of Germans and Russians was apparent. A somewhat more definite relation was observed between infant mortality rates and the percentage of the population born in Poland, the Polish population being associated with high rates, while the percentage of the population born in Canada, England, Scotland and Wales, Ireland, Italy, Austria and Hungary correlated only to a negligible degree with the infant mortality rates of this group of cities.

Several measures of economic status were correlated with infant mortality rates. "Per capita effective income" that is, income received up to $5,000,, showed an extremely low negative correlation; the number of males not filing income tax returns showed a fair degree of correlation with infant mortality rates. A high correlation was obtained when the number of unskilled and semiskilled male laborers per thousand of the male population was used as a measure of economic status.

Among the climatic factors studied, the correlation between infant mortality rates and mean annual temperature was practically zero. Higher correlations were obtained when particular months were studied, low temperatures during February and March being associated with high infant mortality rates to only a slight degree, and high temperatures during July, August and September, to a rather marked degree. These relations between the temperatures of winter and summer months were of the same order when the average mean temperature of January, February and March (1921-1925), and the average mean temperature of July, August and September were correlated with infant mortality rates.

The study of the relation between infant mortality rates and the percentage of possible sunlight was limited to a group of fifty-nine cities having United States Weather Bureau Stations. The correlation between the average percentage of possible sunlight and the average

TABLE 2.—*Simple Correlation Between Infant Mortality Rates and Selected Factors in Ninety-Three Cities of the United States from 1921 to 1925*

Correlated Variables	Coefficient of Correlation
Infant mortality rates (1921-1925) and	
Percentage of illiterate in total population 1920	0.5640
Rainfall (mean annual precipitation), 1921-1925	0.5293
Percentage of Scandinavian birth in total white population, 1920	—0.4672
Number unskilled and semiskilled male laborers per 1,000 male population, 1920	0.4618
Percentage of colored people in total population, 1920	0.3728
Average mean summer temperature (July, August, September), 1921-1925	0.3362
True birth rate, 1921-1925	0.2733
Percentage of married women 15 years of age and over gainfully occupied, 1920	0.2383
Percentage of Polish birth in total white population, 1920	0.1831
Average mean winter temperature (January, February, March), 1921-1925	—0.1621

infant mortality rates of these cities for the period from 1921 to 1925 was extremely low. The amount of rainfall, taken as an indirect measure of the amount of sunlight, showed, on the other hand, a marked correlation with the infant mortality rates of the original ninety-three cities.

A high correlation was observed between infant mortality rates and the percentage of illiteracy in the population. Occupational status of married women, measured by the percentage of married women 15 years of age and over who were gainfully occupied, showed a definite relation to infant mortality rates.

Both crude and true birth rates showed a fair degree of correlation with infant mortality rates.

The correlation between the infant mortality rates and certain of the factors already referred to, resulting in low and high correlation coefficients, is shown in table 2. It will be recalled that the values of the coefficient of correlation range from zero, indicating no relationship between the variables correlated, to unity, indicating perfect relationship. In this table, a high coefficient of correlation, if positive, shows the

tendency of high average infant mortality rates to be associated with high values of the specified correlated factor, that is, with high true birth rates, high illiteracy, large numbers of unskilled and semiskilled laborers etc. If the coefficient is negative, the tendency for high infant mortality rates to be associated with low values of the specified correlated factor, is indicated.

If the correlations between infant mortality rates and the average mean temperature of January, February and March and the percentage of the population of Polish birth are excluded, eight factors remain which correlate with infant mortality rates to an amount indicated by coefficients of 0.2 and over. Some of these factors, however, are significantly correlated with each other. For example, the true birth rate shows a marked correlation with the percentage of illiteracy. The average mean temperature of July, August and September shows a high correlation with the percentage of colored people in the population. The percentage of married women over 15 years of age who are gainfully employed also shows a high correlation with the percentage of colored people and the percentage of illiterate persons. Furthermore, these factors, true birth rate, average summer temperature and percentage of married women gainfully occupied, are highly intercorrelated with factors which in themselves show higher correlations with infant mortality rates. On the basis of such considerations it was decided that the factors showing the most significant correlations with infant mortality rates were: average mean annual precipitation (1921 to 1925), number of unskilled and semiskilled male laborers per 1,000 male population, percentage of colored people, percentage of Scandinavians and percentage of illiterate persons.

Reference to the coefficients of correlation between the average infant mortality rates of ninety-three cities from 1921 to 1925 and the factors given in table 2 shows that the highest correlation obtained was that between average infant mortality rates and the percentage of illiterate persons in the population, the coefficient having a value of 0.5640. If these factors are correlated with average infant mortality rates in various combinations, "in multiple," coefficients of multiple correlation ranging from 0.6922 to 0.7365 are obtained. No one of these factors correlates as highly with infant mortality rates as all of the factors taken in combination.

The effect of combining these factors variously in correlations with infant mortality rates is shown in table 3, which gives the multiple correlation coefficients for various groupings of the factors.

The highest coefficient of multiple correlation is obtained when all five factors, average mean annual precipitation, number of unskilled and semiskilled male workers per thousand of the male population, percentage of colored people, percentage of Scandinavians and percentage of

illiterate persons taken as a unit, are correlated with infant mortality rates. The factor number of unskilled and semiskilled male workers per thousand of the male population contributes most to this coefficient, since its omission causes the greatest reduction in the coefficient of multiple correlation. The factor mean annual precipitation appears to contribute least weight, since its omission reduces the coefficient of multiple correlation between average infant mortality rates and the total group of five factors slightly (in the third and fourth decimal places).

The correlations made in this investigation have made it possible to select from the many factors affecting infant mortality rates five so-called "external" factors which, taken in various combinations, correlate with infant mortality rates to the extent indicated by the multiple correlation coefficients from 0.6922 to 0.7365. While these coefficients do not indicate the solution of the problem of the cause of variation in infant mortality rates, they are of value as a quantitative demarcation of known from unknown factors which affect infant mortality. Practically, they forecast the degree of correlation of actual infant mortality rates with those predicted by regression equations of infant mortality rates on these factors.

TABLE 3.—*Multiple Correlation Between Infant Mortality Rates and Factors Showing Significant Simple Correlation in Ninety-Three Cities of the United States from 1921 to 1925*

Correlated Variables	Coefficient of Multiple Correlation
Infant mortality and	
Rainfall, number unskilled workers, percentage colored, percentage Scandinavian, percentage illiterate	0.7365
Number unskilled workers, percentage colored, percentage Scandinavian, percentage illiterate	0.7336
Rainfall, number unskilled workers, percentage colored, percentage Scandinavian	0.7189
Rainfall, number unskilled workers, percentage Scandinavian, percentage illiterate	0.6992
Rainfall, number unskilled workers, percentage colored, percentage illiterate	0.6954
Rainfall, percentage colored, percentage Scandinavian, percentage illiterate	0.6922

THE REGRESSION EQUATION AND THE PREDICTION OF INFANT MORTALITY RATES

The largest of the coefficients of multiple correlation listed in table 3 is that showing the correlation between infant mortality rates and the five factors: mean annual precipitation, number of unskilled and semiskilled male laborers per thousand of the male population, percentage of colored people, percentage of Scandinavians and percentage of illiterate persons. A regression equation based on these factors should, then, predict infant mortality rates which will give the highest correlation with the actual rates; however, when the factor mean annual precipitation is

omitted from this group, the coefficient is only slightly reduced. Since the ease of use of the regression equation will be greater the fewer the factors used, it was decided to present the regression equation using the four variables: number of unskilled and semiskilled male laborers per thousand of the male population, percentage of colored people, percentage of Scandinavians and percentage of illiterate persons, and omitting mean annual precipitation. The predictions of this regression equation will be practically as useful as those based on the equation with five factors.

If $\times_1$ is the average infant mortality rate (1921 to 1925), $\times_2$ the percentage of unskilled and semiskilled male workers per thousand of

TABLE 4.—*The Use of the Regression Equation in the Prediction of Infant Mortality Rates; Examples Selected to Show Agreement and Disagreement Between Predicted and Actual Infant Mortality Rates (1921-1925)*

Designation of City	X_2 Number of Unskilled and Semiskilled Male Laborers per 1,000 Male Population, 1920	X_3 Percentage of Colored in Total Population, 1920	X_4 Percentage of Scandinavian Birth in Total White Population, 1920	X_5 Percentage of Illiterate in Total Population, 1920	X_2 × 0.0677	+ X_3 × 0.4141	− X_4 × 1.2459	+ X_5 × 0.9724	+ 57.2	= X_1 Infant Mortality Rates, Average 1921-25 Predicted	Actual
1	205	1	15	4	13.9	0.4	18.7	3.9	57.2	57	64
2	133	1	12	2	9.0	0.4	14.9	2.0	57.2	54	56
3	64	1	4	1	4.3	0.4	5.0	1.0	57.2	58	63
4	183	30	0	11	12.4	12.4	0	10.7	57.2	93	91
5	347	4	0	15	23.5	1.7	0	14.6	57.2	97	93
6	166	32	0	11	11.2	13.3	0	10.7	57.2	92	87
7	153	1	13	3	10.4	0.4	16.2	2.9	57.2	55	68
8	177	3	1	2	12.0	1.2	1.2	1.9	57.2	71	82
9	137	2	1	5	9.3	0.8	1.2	4.9	57.2	71	82
10	80	1	2	1	5.4	0.4	2.5	1.0	57.2	62	43
11	90	2	2	1	6.1	0.8	2.5	1.0	57.2	63	41
12	288	22	0	7	19.5	9.1	0	6.8	57.2	93	72

the male population (1920), $\times_3$ the percentage of colored people (1920), $\times_4$ the percentage of Scandinavians (1920) and $\times_5$ the percentage of illiterate persons (1920), then this regression equation in terms of original values, is as follows: $\times_1 = 57.2137 + 0.0677\times_2 + 0.4141\times_3 - 1.2459\times_4 + 0.9724\times_5$. The use of this equation in the prediction of infant mortality rates is demonstrated in table 4.

In the first four columns are given the figures from the census of 1920 of the number of unskilled male laborers, percentage of colored people, percentage of Scandinavian birth and percentage of illiterate persons for twelve cities selected from the total group of ninety-three. These figures are multiplied by the coefficients of regression calculated for each specific factor. For example, $\times_2$, the number of unskilled and semiskilled male laborers per thousand of the population of city 1 is 205. The coefficient of net regression for this variable is 0.0677. If 205 is multiplied by

TABLE 5.—*Predicted and Actual Infant Mortality Rates of Ninety-Three Cities in the United States from 1921 to 1925*

Name of City	Data on Which Rates Were Predicted Census of 1920				Infant Mortality Rates, Average 1921-1925	
	Number of Male Laborers* per 1,000 Male Population	Percentage of Colored in Total Population	Percentage of Scandinavian Birth in Total White Population	Percentage of Illiterate in Total Population	Predicted	Actual
Berkeley	80	1	2	1	62	43
Los Angeles	123	3	2	2	66	69
Oakland	160	3	3	3	69	59
Pasadena	90	2	2	1	63	41
Sacramento	150	1	1	3	70	71
San Diego	101	1	2	2	64	55
San Francisco	118	1	3	2	64	55
Stockton	156	1	1	3	70	71
Hartford	181	3	2	6	74	76
New Haven	163	3	1	8	76	70
Waterbury	224	1	1	10	81	83
Wilmington	209	10	0	7	82	94
Washington, D.C.	100	25	0	3	77	85
Jacksonville	178	45	0	7	95	86
Tampa	288	22	0	7	93	72
Chicago	161	4	3	6	72	81
Decatur	177	3	0	2	72	76
Peoria	177	3	1	2	71	82
Rockford	205	1	15	4	57	64
Springfield	217	5	0	3	77	81
Evansville	205	8	0	3	77	75
Fort Wayne	171	2	0	2	72	62
Indianapolis	175	11	0	3	77	77
South Bend	251	2	1	5	79	68
Terre Haute	223	6	0	2	77	81
Topeka	123	9	1	3	71	76
Wichita	136	5	0	1	70	69
Lexington	183	30	0	11	93	91
Louisville	175	17	0	5	81	78
Portland, Maine	103	0	1	3	66	73
Baltimore	173	15	0	6	81	86
Boston	137	2	1	5	71	82
Fall River	318	0	0	16	94	103
Fitchburg	263	0	1	6	80	77
Lawrence	363	0	0	12	94	76
Lowell	269	0	1	9	83	95
New Bedford	347	4	0	15	97	93
Worcester	193	1	4	6	72	74
Bay City	209	0	1	5	75	73
Grand Rapids	190	1	1	4	73	63
Jackson	207	2	0	3	75	81
Kalamazoo	211	2	0	3	75	66
Lansing	244	1	0	2	76	77
Saginaw	186	1	0	3	73	82
Duluth	153	1	13	3	55	68
Minneapolis	133	1	12	2	54	56
St. Paul	140	1	6	2	62	60
Butte	323	1	3	3	79	81
Lincoln	102	2	1	3	67	61
Omaha	171	5	4	3	69	71
Atlantic City	77	22	0	3	75	82
Elizabeth	187	2	0	8	79	65
Jersey City	148	3	1	6	73	78
Paterson	243	1	0	8	82	70
Trenton	263	4	0	9	85	88
Albany	120	1	0	4	70	80
Binghamton	230	1	0	4	77	75
Buffalo	162	1	0	5	74	91
Elmira	153	1	0	3	71	80
Mount Vernon	84	3	1	6	69	58
New York	123	3	1	8	74	69
Rochester	202	1	0	6	77	70
Syracuse	168	1	0	5	74	78
Charlotte	166	32	0	11	92	87
Canton	240	2	0	5	79	76
Cincinnati	170	8	0	2	74	77
Cleveland	193	4	0	7	79	70
Columbus	162	9	0	3	75	77
Dayton	183	6	0	2	74	70
Lima	142	3	0	2	70	70
Toledo	190	2	0	3	74	75
Portland, Ore	151	1	4	2	65	52
Altoona	127	2	0	3	71	73
Erie	212	1	1	7	78	67
Harrisburg	136	7	0	3	72	78

* Unskilled and semiskilled.

TABLE 5.—*Predicted and Actual Infant Mortality Rates of Ninety-Three Cities in the United States from 1921 to 1925—Continued*

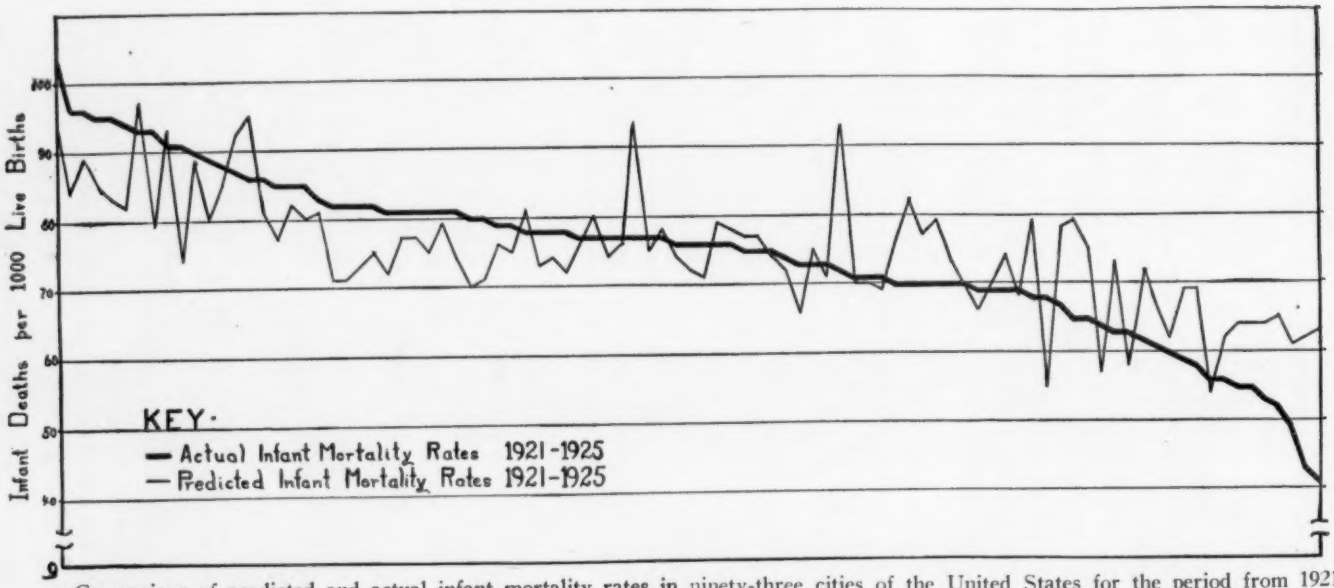
Name of City	Data on Which Rates Were Predicted Census of 1920				Infant Mortality Rates, Average 1921-1925	
	Number of Male Laborers* per 1,000 Male Population	Percentage of Colored in Total Population	Percentage of Scandinavian Birth in Total White Population	Percentage of Illiterate in Total Population	Predicted	Actual
Johnstown	302	3	0	5	84	96
Lancaster	212	2	0	2	74	81
New Castle	238	2	0	8	82	85
Philadelphia	169	7	0	5	76	79
Pittsburgh	200	6	0	6	79	93
Reading	266	1	0	4	80	85
Scranton	280	0	0	9	85	95
York	252	3	0	2	78	76
Providence	193	2	1	8	78	77
Salt Lake City	64	1	4	1	58	63
Norfolk	122	38	0	8	89	90
Richmond	178	32	0	7	89	96
Roanoke	136	18	0	6	80	89
Seattle	152	1	7	2	61	49
Spokane	117	1	4	1	62	56
Tacoma	191	1	7	2	64	53
Milwaukee	197	1	0	4	75	79
Racine	252	1	8	3	68	69

* Unskilled and semiskilled.

0.0677, the result, 13.9, will be the amount which this factor contributes to the predicted infant mortality rate. Columns 5, 6, 7 and 8 give the results of such multiplications. In each case, the constant amount, 57.2, must be added; the final result, then, is the predicted infant mortality rate.

The predicted and actual average infant mortality rates for the period from 1921 to 1925 for the ninety-three cities studied, so calculated, together with the data for the four factors used in the regression equation, are given in table 5. When the predicted rates were correlated with the actual rates, the coefficient of correlation was found to be 0.7338. This coefficient checks closely with the coefficient of multiple correlation between the average infant mortality rates and the factors used in the regression equation, which was 0.7336. It is also of interest to note that the coefficient of correlation between these predicted rates and the actual average infant mortality rates of the ninety-three cities for the years from 1925 to 1927 was 0.6903; for the year 1925, 0.6174; for 1926, 0.6794, and for 1927, 0.4866.

The lower coefficients in these later years are probably due to the fact that the data used in the regression equation were as of 1920, and therefore increasingly inaccurate in the later years of this decade. Figures for one year will, of course, be less accurate than the five year average on which the computations were based. In addition, any calculations based on infant mortality rates during 1926 and 1927 necessarily involve the error due to the use of provisional infant mortality rates.



Comparison of predicted and actual infant mortality rates in ninety-three cities of the United States for the period from 1921 to 1925.

The predicted and actual average infant mortality rates for the period from 1921 to 1925 for the ninety-three cities included in this study have been plotted in the accompanying chart.

Specific examples of agreement and disagreement between the predicted and actual average infant mortality rates were selected for presentation in table 4. Close agreement between the predicted and actual infant mortality rates is shown in cities 1 to 6. In the first three, both the predicted and the actual infant mortality rates are low; in cities 4 to 6, both the predicted and the actual infant mortality rates are high. Cities 7 to 12 are selected examples of disagreement between the predicted and the actual infant mortality rates. The rates predicted for cities 7 to 9 are lower than the actual; those predicted for cities 10 to 12 are higher than the actual.

In the cases in which there is close agreement between predicted and actual rates (cities 1 to 6), the four factors listed—number of unskilled and semiskilled male laborers, percentage of colored people, percentage of Scandinavians and percentage of illiterate persons—probably are adequate measures of the underlying "internal" causes of infant mortality. In the cities in which disagreement is shown, these factors are inadequate or incomplete in number, and other factors must be sought to explain the amount by which actual rates deviate from predicted rates. It seems likely, for example, that the number of unskilled and semiskilled male laborers would fail to measure adequately the economic status of cities in which the extent of poverty or wealth was extreme.

SUMMARY

This investigation was undertaken to determine the nature of the local and sectional characteristics which influence infant mortality, and to apply the observations of this preliminary study in the prediction of infant mortality rates which measure quantitatively the effect of these factors.

The preliminary correlation of a series of factors with the infant mortality rates of ninety-three American cities for the period from 1921 to 1925 has shown:

(1) That climatic factors, such as temperature, rainfall and sunlight are relatively unimportant in their effect on urban infant mortality;

(2) That race is an important factor; nativity, except of one foreign-born group, the Scandinavians, being of comparatively slight relation to infant mortality in the ninety-three cities studied, taken as a group and

(3) That economic and educational status are of great importance in their effect on urban infant mortality.

An equation based on a group of four factors, including the number of unskilled and semiskilled male laborers per thousand of population,

percentage of colored people, percentage of Scandinavian birth and percentage of illiterate persons, was used to compute the infant mortality rates determined by these factors in ninety-three cities of the United States. These "predicted" rates may be considered tentative "minimum" infant mortality rates.

This study has revealed the relative degree of association of certain external factors with infant mortality rates, and the feasibility of predicting rates from certain indexes of external influences. A table of predicted rates for experimental purposes is offered for ninety-three cities.

JOHN LOCKE, PEDIATRICIAN *

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Dominating the field of pediatric literature, during the latter part of the seventeenth century, were two treatises, the "De Rachitide" (1650) of Glisson, and Walter Harris', "De Morbis Acutis Infantum." The theories of the latter regarding "puerile humidity" and its resulting "acid putrefaction" as the cause of disease in childhood, were accepted almost universally, as evidenced by the numerous English editions and Continental translations through which his work passed subsequent to its first appearance in London in 1689. Not until a century later did Michael Underwood bring forth his "Treatise on the Disease of Children" (1789), and place the study of disease of childhood on a rational basis.

Considering the curious theories and therapeutic vagaries prevalent in this period, it is of interest to come on a work published during this interim which deals with children and their bringing up and yet fosters none of the mistaken notions of its contemporaries, but deals with the problems of childhood in a manner thoroughly modern. The title of this surprising volume is "Some Thoughts Concerning Education," and its author was England's great metaphysician, John Locke. His "Essay on Human Understanding" is much more widely known than his book on education, but the latter work manifests the ability of its author to think logically and independently when dealing with a matter obscured by many fallacies and fancies.

Locke was born in Somerset, England, in 1632, and at 14 years of age was placed by his father in Westminster School under Dr. Busby. In 1652, he entered Christ Church, Oxford, and had conferred on him the degree of B.A. in 1655. Continuing his academic course, he was granted the degree of M.A. in 1658, and, although he never took the doctor's degree in medicine, he obtained the bachelor's degree in this subject in 1674, holding one of the two medical studentships at Christ's Church.

The elder Locke dealt rather sternly with his son in his youth, but as adolescence and young manhood were attained, there came about a gradual admission to paternal friendship. Locke loved his father dearly,

* Received for publication, July 27, 1928.

and the early rigors at his parent's hands served only to make him the more grateful for the excellence of the training he received. Influenced, no doubt, by the manner in which he was brought up, Locke seems to have devoted a considerable measure of thought to the early training of children. A full realization of the debt he owed his parent is expressed in a letter written before he was 30 years of age, to his father who had been ill. In concluding the letter he said:

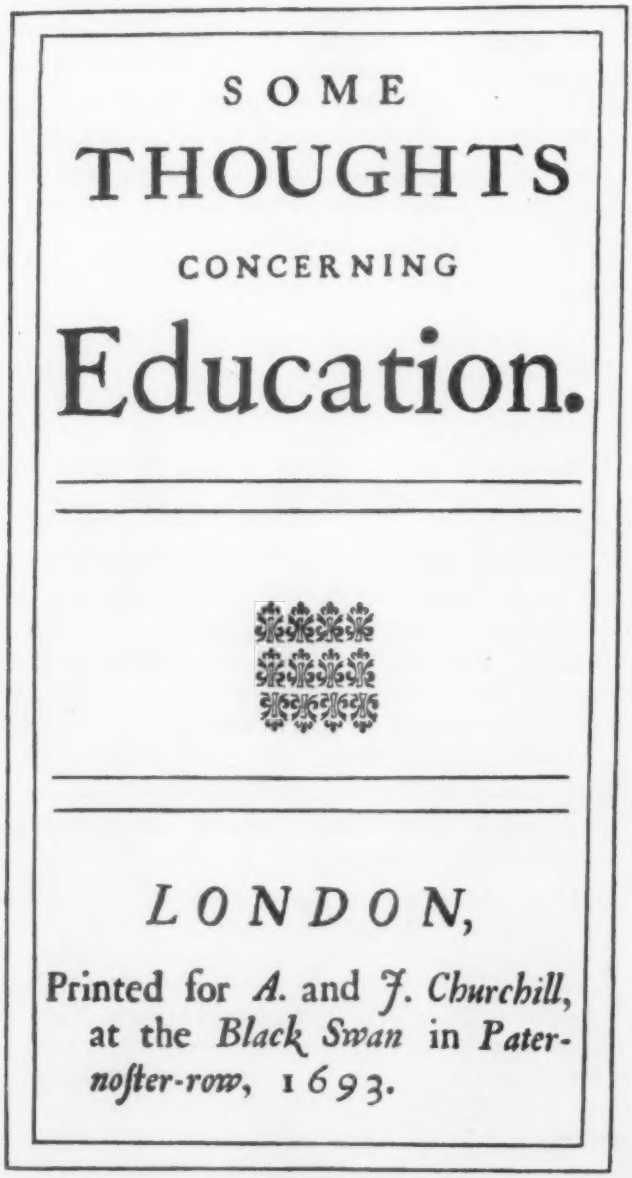
> No thoughts, how important soever, shall make me forget my duty; and a father is more than all other relations; and the greatest satisfaction I can purpose to myself in the world, is my hopes that you may yet live to receive the return of some comfort, for all that care and indulgence you have placed in,
> Sir, your most obedient son, J. L.

There are many evidences that Locke was not only fond of children, but that he also numbered many little folk among his patients. Notations dealing with his opinions regarding the diseases of some of his younger patients are to be found in the biography of Locke by Fox-Bourne, and his conservative attitude in the treatment of children is plainly delineated in those portions of the "Thoughts Concerning Education" which deal with "Physic."

In 1667, Locke joined the household of Lord Ashley, later Earl of Shaftesbury, and for the greater part of the succeeding seventeen years, was confident and advisor of his patron, as well as physician and tutor to the household. Contacts with children were readily made under the circumstances of his position in Ashley's home, and the instance of Locke's friendship for the son of Mr. T. Stringer, Lord Ashley's secretary, may be noted as characteristic. Mr. Stringer had a cottage in the country, where Locke used to visit him frequently, and the following notations in his diary for 1679 show plainly how anxious he was to please the small son of his host:

> Paid, 1s. 6d. for a drum for little T. Stringer.
> Paid for playthings for little Stringer, 3s.

"The Thoughts Concerning Education" was published in London, in 1693, as a small octavo of 262 pages, bound in calf. The title page is shown in figure 1, and, strangely enough, Locke's name does not appear on it, nor does it appear at the end of the "epistle dedicatory" addressed to his friend Edward Clarke. Written ten years before their publication, the letters of which the book is composed were sent to Clarke from Holland, where Shaftesbury and Locke found it convenient to remain during the latter part of 1683, in order to escape the displeasure of the Court. The purpose of the correspondence was to supply Clarke with a guide which he could follow in the education of his son, and the


SOME
THOUGHTS
CONCERNING
Education.

LONDON,
Printed for A. and J. Churchill, at the Black Swan in Pater-noſter-row, 1693.

Fig. 1.—Title page.

work throughout reveals a sagacious regard for the building of character, and stresses wisdom of a practical nature as of more importance than learning.

The book is not divided into chapters, but consists of a succession of 202 numbered sections, for each of which are subject guides of one word printed out in the margin of the page. After noting that 'men's happiness or misery is most part of their own making,' Locke claimed that of all the men we meet, nine of ten are what they are, good or evil, useful or not, by their education, and, believing in the dictum of a sound mind in a sound body, he proceeded to outline the regimen to be followed in order that a child might be healthy.

> The consideration, I shall here have of health, shall be, not what a physician ought to do with a sick or crazy child; but what the parents, without the help of physic, should do for the preservation and improvement of an healthy or at least not sickly constitution in their children: And this perhaps might be dispatched, all in this one short rule; viz., that gentlemen should use their children, as the honest farmers and substantial yeomen do theirs. But because the mothers possible may think this a little too hard, and the fathers too short, I shall explain myself more particularly, only laying down this as a general and certain observation for the women to consider, viz., that most children's constitutions, are either spoiled or harmed by cockering and tenderness. The first thing to be taken care of, is, that children be not too warmly clad or covered winter or summer. The face, when we are born, is no less tender than any other part of the body: 'tis use alone hardens it, and makes it more able to endure the cold; and therefore the Scythian philosopher gave a very significant answer to the Athenian, who wondered how he could go naked in frost and snow. How, said the Scythian, can you endure your face exposed to the sharp winter air? My face is used to it, said the Athenian. Think me all face replied the Scythian. Our bodies will endure anything, that from the beginning they are accustomed to. And therefore, amongst other things, I think that when Nature has so well covered his head with hair, and strengthened it with a year or two's age, that he can run about, by day, without a cap, it is best, that by night a child should also lie without one, there being nothing that more exposes to headache, colds, catarrhs, coughs, and several other diseases, than keeping the head warm.

The delightfully irrefutable logic of the gradual development toward the statement in the last sentence quoted, even to its "and therefore," is very suggestive of the mental processes of the mathematician, in the demonstration of his theorem.

After explaining that the word "he" was employed because the discourse concerns chiefly young gentlemen, and not daughters, "though where the difference of sex requires different treatment 'twill be no hard matter to distinguish.' The matter of shoes for the gentleman was considered.

> I would also advise his feet to be washed every night in cold water; and to have his shoes so thin, that they might leak and let in water, whenever he comes near it. Here, I fear, I shall have the mistress and maids too, against me; the

one will think it too filthy, and the other, perhaps, too much pains to make clean his stockings. But yet truth will have it, that his health is much more worth than all such considerations and ten times as much more. And he that considers how mischievous and mortal a thing, taking wet in the feet is to those, who have been bred nicely, will wish he had, with the poor people's children,

Fig. 2.—John Locke.

gone barefoot; who, by that means, come to be so reconciled, by custom, to wet in their feet, that they take no more cold or harm by it, than if they were wet in their hands.

Playing out of doors so that a child's body might become accustomed to heat and cold, as well as sunshine and rain, was deemed practical by Locke.

If I should advise him to play in the wind and sun without a hat, I doubt whether it could be born; there would a thousand objections be made against it, which at last would amount to no more, in truth, than being sunburnt; and if my young master is to be kept always in the shade, and never exposed to the sun and wind, for fear of his complexion, it may be a good way to make him a beau, but not a man of business.

After advising mothers to refrain from the use of tight clothes, and all straight lacing, Locke passed next to the subject of diet, in the first portion of which he stated:

As for his diet, it ought to be very plain and simple. Flesh once a day, and of one sort at a meal, is enough. Beef, mutton, veal, etc., without other sauce than hunger, is best; and great care should be used, that he eat bread plentifully, both alone and with everything else. And whatever he eats that is solid, make him chew it well. We English are often negligent herein; from whence follow indigestion, and other great inconveniences. For breakfast and supper milk, milk-pottage, water-gruel, flummery, and twenty other things that we are wont to take in England, are very fit for children. . . . . If he at any time calls for victuals between meals, use him to nothing but dry bread; if he be hungry more than wanton, bread alone will down; and if he be not hungry, 'tis not fit he should eat.

Perhaps the prescribed diet is a bit strict, but the reasons assigned for maintaining its simplicity are convincingly and sincerely presented, and there is no hint of "acid putrefaction" as a cause of disease. However, modern advocates of regularity in the arrangement of hours for meals, will probably object strenously to Locke's advice in the matter which follows:

As to his meals, I should think it best, that, as much as can be conveniently avoided, they should not be kept constantly to an hour; for when custom has fixed his eating to certain stated periods, his stomach will expect victuals at the usual hour; and if he passes it, either grow indisposed, and as it were peevish, or lose its appetite. . . . . If anyone think this too hard and sparing a diet for a child, let them know, that a child will never starve, nor want nourishment, who, besides flesh once a day, and other things once or twice more, may have good bread and beer as often as he had a stomach.

Several sections are devoted to the subject of drink, emphasis being laid on the fact that having 'the cup often at his nose' is a dangerous beginning and preparation to good fellowship. Although small beer is considered not harmful, wine and strong drink are forbidden, and parents are warned against allowing servants to tempt the young master with that which they themselves enjoy so well.

Regarding the use of fruits in a child's diet, he advised:

Melons, peaches, most sorts of plums, and all sorts of grapes in England, I think children should be wholly kept from, as having a very tempting taste, in a very unwholesome juice; so that, if it were possible, they should never so much as see them, or know there were any such thing. But strawberries,

cherries, gooseberries, or currants, when thorough ripe, I think may be very safely allowed them, and that with a pretty liberal hand. . . . . and children should have them for their breakfasts.

Of sleep, children should have 'their full satisfaction,' and early rising and retiring hours are advised that a youth may not waste his time in lying abed in drowsiness, nor become accustomed to the unsafe hours of debauchery which are those of the evening.

Under the heading of "costiveness," the admonitions seem hardly those of a man writing in 1693. Yet Locke advised early training in the matter of regularity of going to stool and gave an account of observations and experiments, which proved conclusively to his mind that the establishment of regular habit in this matter is purely a question of individual training.

Most surprising of all the sections in Locke's book is the one dealing with physic. It is remarkable that one living in a time of heroic dosages and innumerable medications could arrive at so sane a discussion of the question of medication for children as he presents in the following paragraphs:

This is all I have to trouble you with concerning his management, in the ordinary course of his health; and perhaps it will be expected from me, that I should give some directions of physic to prevent diseases. For which I have only this one very sacredly to be observed: Never to give children any physic for prevention. . . . . Nor even upon every little indisposition is physic to be given, or the physician to be called to children, especially if he be a busy man, that will presently fill their windows with gally-pots, and their stomachs with drugs. . . . . It seeming suitable both to my reason and experience, that the tender constitutions of children, should have as little done to them, as is possible, and as the absolute necessity of the case requires. . . . . When such a gentle treatment will not prevent the growing mischief, but that it will turn into a formed disease, it will be time to seek the advice of some sober and discreet physician. In this part, I hope, I shall find an easy belief, and nobody can have a pretense to doubt the advice of one, who has spent some time in the study of physic, when he counsels you not to be too forward in making use of physic and physicians.

Perhaps the best summary of John Locke's advice to Clarke can be given by allowing the author to speak for himself by quoting the thirtieth paragraph.

And thus I have done with what concerns the body and health, which reduces itself to these few and easily observable rules. Plenty of open air, exercise and sleep; plain diet, no wine or strong drink, and very little or no physic; not too warm and straight clothing, especially the head and feet kept cold, and the feet often used to cold water, and exposed to wet.

LIKENESSES AND CONTRASTS IN THE HEMOLYTIC ANEMIAS OF CHILDHOOD*

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DETROIT

There are three diseases of early childhood, apparently rather closely related not only in symptomatology but probably also in fundamental etiology, which to my mind are of peculiar interest because of the opportunity which they seem to offer for the solution of some of the intriguing problems presented by the hemolytic anemias, which now interest many in the medical profession.

These three diseases are: congenital hemolytic icterus, sickle-cell anemia and the disease which I have attempted to define in a previous paper [1] and which has hitherto been included under the rather vague classification of von Jaksch's anemia. In my paper on this subject, for reasons there given, I suggested leaving it under that title, in spite of the fact that I did not believe it to be the disease which von Jaksch was describing, if indeed he had in mind anything which would now be considered a clinical entity. Further reflection has convinced me that I was wrong not to urge its recognition under a new name. Difficulty in coining an appropriate name had something to do with my conclusion not to attempt a change at that time; but as I have come to feel that for clarity of conception the disease must be better distinguished, I am inclined now to suggest that it be known by what seems to be its most striking hematologic characteristic, namely, the extremely large number of erythroblasts to be found in the circulating blood, especially after splenectomy. For my own purposes, therefore, I shall speak of it hereafter as the erythroblastic anemia of childhood.

In this paper it is my purpose to point out essential likenesses and differences between these three anemias, and to theorize somewhat as to the causes of these and their possible application to the study of the hemolytic diseases.

The symptomatology of all three has been discussed so thoroughly that I assume it to be familiar to any one interested, and I omit any details not pertinent to my own thesis.

In all three conditions, one must recognize either a congenital disease or a pronounced and peculiar congenital diathesis. Hemolytic jaundice and sickle-cell anemia are definitely hereditary and familial, at least, as to

* Received for publication, Sept. 21, 1928.

1. Cooley, T. B.: Von Jaksch's Anemia, Am. J. Dis. Child. **33**:786 (May) 1927.

diathesis. The erythroblastic anemia is not known to be hereditary, for which there is an obvious probable explanation in the fact that its subjects are not known to reach adult life. It is, however, often familial.

Sickle-cell anemia is distinctly racial and possibly originally limited to a small section of the negro race. The erythroblastic anemia is so conspicuously more common in the Mediterranean races as to seem almost peculiar to them; while hemolytic jaundice, though more widespread than the other two, tends decidedly to be more frequent in certain regions and among certain people, and to appear only sporadically elsewhere. In other words, in all three the diathesis seems distinctly a matter of family or race.

HEMATOLOGY

There are striking general resemblances in the hematology of the three diseases. The most important, perhaps, is that each seems to be characterized by a peculiar type of red cell. The sickle-cell type may be said to be unique in hematology. Microcytosis was recognized by Gänsslen [2] and by others as characteristic of hemolytic jaundice, and Gänsslen ascribed peculiar qualities to these microcytes. No other disease shows uniformly at its height so many erythroblasts as does the erythroblastic anemia, and after splenectomy their numbers are remarkable. As will appear later, I think they may be a special form of cell.

Hemolytic jaundice is said to show more reticulated red cells than any other disease. There is, however, little difference in this respect between it and the other two; sickle-cell anemia especially, in the active stage, showing extremely large numbers.

Increased fragility of the erythrocytes to hypotonic salt solutions is generally recognized as a cardinal symptom of hemolytic jaundice. It is more common in this disease, but has been observed in both the others. Urobilinuria, also, more common in hemolytic jaundice, may be present in either of the others.

As to the white cells, hemolytic jaundice and sickle-cell anemia do not show any remarkable characteristics. The erythroblastic anemia, the most serious and rapidly progressing, early shows evidence of pronounced bone marrow irritation, which apparently is reflected in the production of increased numbers of leukocytes, with the appearance in the blood of early forms. With the development of marked marrow hyperplasia the numbers of these cells may run to high figures.

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2. Gänsslen, Zipperlen and Schüz: Hemolytic Constitution, Deutsches Arch. f. klin. Med. **146**:1 (Jan.) 1925.

In a former paper, my associates and I [3] called attention to this extreme hyperplasia of the marrow in the erythroblastic anemia. In sickle-cell anemia it is apparently less constant and less pronounced; while in hemolytic jaundice it seems not to have been especially noted, though some reports of peculiarly shaped heads associated with this disease may indicate a similar, slower process.

FUNCTION OF THE SPLEEN

The behavior of the spleen in the three conditions shows both resemblances and differences. In all it must be assumed to have an active part in the hemolytic process, and it is probable that the histologic changes that take place in it are somehow the result of this activity. It is rather peculiar, then, that there should be such differences as may be noted in its size and structure. In hemolytic jaundice, the mildest of the three, it is often little if any enlarged, and is likely to vary in size with the amount of hemolysis going on, being particularly noticeable during the crises, the changes in size being due apparently to variations in the amount of retained blood. Histologically, it shows a moderate fibrosis and an infiltration with erythrocytes. Sickle-cell anemia has similar crises and similar changes in the volume of the spleen. It seems to be true that here the spleen is early enlarged, more or less so according to the activity of the process, but later shrinks to less than normal size, with the development of a peculiar fibrosis, amounting almost to cicatrization. When removed early, its gross appearance is hardly distinguishable from that seen in hemolytic jaundice. In the erythroblastic anemia, the early enlargement is greater than in the other two, and the increase is progressive, with less variation from time to time. The histologic changes here are rather more complex than in the other two. Might it not be possible to explain the differences in structure on the basis of reaction to differing irritants in the products of the peculiar cells destroyed in the three conditions?

Removal of the spleen has different results in the three diseases. In hemolytic jaundice, with the exception of rare cases of the pernicious type, the result is usually almost, if not quite, a complete cure. Without any remarkable immediate reaction, hemolysis stops or is greatly diminished, the anemia and jaundice disappear and the patient is to all intents well.

In sickle-cell anemia, after early splenectomy, there is again no pronounced immediate reaction. Normoblasts, often present in considerable numbers before the operation, tend to disappear, while at the same time reticulation may be increased. The patient seems somewhat

3. Cooley, T. B.; Witwer, E. R., and Lee, Pearl: Anemia in Children with Splenomegaly, Am. J. Dis. Child. **34**:347 (Sept.) 1927.

improved, particularly in the sense that crises are less frequent, and the anemia is less pronounced; but hemolysis is still observed, and after the first decrease is likely to increase again. Sickling is unchanged.

In the erythroblastic disease, splenectomy is followed by a remarkable increase of erythroblasts in the blood, lasting over years; but so far as available reports are concerned, there seems to be little definite improvement in the patient. Hemolysis and jaundice, if present, may be temporarily lessened, but they return and the disease process continues as before. The benefit to the patient lies mostly in the removal of the drag of the heavy spleen.

In other words, from the simplest to the most severe disease there is progressively less benefit from the removal of the organ supposed to be chiefly concerned in hemolysis. Why?

Adequate knowledge of the functions of the spleen and its relation to blood formation and destruction in health and disease is still much lacking. A multiplicity of theories has been advanced which I cannot discuss here. It must, I think, be admitted that the spleen is primarily and chiefly involved in the mechanism of blood destruction, and that a secondary influence is exerted by the rest of the reticulo-endothelial system. The simplest explanation of the relation of the spleen to the hemolytic anemias is that it destroys in abnormal numbers red cells which have in some way become especially vulnerable. The changes in the spleen itself are, according to this theory, supposed to be due to its abnormal activity. Various objections have been made to this theory, which, however, seems to me to fit better than any other for hemolytic jaundice. It does not, however, without modification, seem to apply very well to sickle-cell anemia, the erythroblastic anemia, or the pernicious anemia of adults in all of which splenectomy is of less definite benefit. I am inclined to offer a further theory which seems to me plausible as an explanation of this difference in the effects of splenectomy. I have spoken of the three anemias under discussion as characterized each by a peculiar cell. My theory assumes that these cells are abnormal in structure, and that if their destruction is stopped or minimized by splenectomy, the patient is benefited only in so far as the cells thus left in circulation are capable of functioning in a normal way. It may well be that the microcyte, if that is the characteristic abnormal cell of hemolytic jaundice, is more useful than the sickle cell, the nucleated forms of the erythroblastic anemia, or those that characterize pernicious anemia, with which the erythroblastic disease has much in common. Hahn and Gillespie[4] have expressed a similar idea with regard to sickle-cell anemia.

4. Hahn, E. V., and Gillespie, E. B.: Sickle Cell Anemia, Arch. Int. Med. **39**:233 (Feb.) 1927.

Another vexing question is: Why, in all these diseases, except hemolytic jaundice, is hemolysis so little diminished by splenectomy? In accordance with my assumption one must suppose that hemolysis after splenectomy is carried on by the other parts of the reticulo-endothelial system, and further that in hemolytic jaundice the peculiar cells, less abnormal than those of the other two, have less stimulating action on these accessory hemolytic organs.

COMMENT

It would seem to me, then, that these diseases might be thought of as three types of hemolytic jaundice, each dependent on a congenital diathesis, and each strikingly limited to familial or racial groups. Further, I would suggest that each is characterized by a peculiar, abnormal type of red cell, and that much of the clinical symptomatology is due to hemolysis of these abnormal cells under the influence of the spleen and its associated tissues. Either physical or chemical abnormalities in cell structure might be the reason for this increased susceptibility to hemolysis, and the observations of Hahn and Gillespie [4] with respect to the sickle cell, the most definite there are, do not show positively where the fault lies. Gänsslen's conception of the microcyte as a cell that is more spherical than biconcave, and for that reason more vulnerable, would fit either idea. Concerning the nucleated cells of the erythroblastic anemia, there is at present no special information, except that their behavior after splenectomy suggests the possibility that they are a different form from those observed during periods of regeneration in other anemias.

If there is a group of congenital diseases characterized by the production of red cells defective in physical or chemical structure, to what might these structural defects be ascribed? The idea of toxins, which so long had a prominent place in the theories of pernicious anemia, seems somewhat less in evidence in the current literature, and could hardly have any application to the conditions under discussion. Congenital abnormalities in the erythropoietic bone marrow would be a plausible explanation, especially for peculiarities of physical structure, and could not at present be ruled out. Another possibility, which certainly deserves attention, is that the failure of the bone marrow may result from an inadequate supply of proper material for blood-making —that it is endeavoring to make "bricks without straw." Present results in the treatment of pernicious anemia point strongly to this assumption. The inadequate supply might be due to defective absorption, or to some failure in the intermediate metabolism, whether or not due to a "hormone" deficiency.

A good deal is being done in the study of the chemistry of the blood fluids, but I think that there is a decided need for more information than there is now regarding the physical structure and the finer chemistry of the red cell, in health and in disease, and that study of these subjects will be an important step in the elucidation of the problem of the hemolytic anemias. So far as disease processes go, the sickle-cell diathesis offers an ideal field for this study, as, in many subjects, practically all the red cells are abnormal. The work of Hahn and Gillespie should serve as the basis for further important investigations.

Pediatric Biographies

GUILLAUME DE BAILLOU (BALLONIUS)
1538-1616 *

JOHN RUHRÄH, M.D.
BALTIMORE

De Baillou is an important figure in medicine, and as he was the first physician to describe whooping cough, he deserves to rank high among those who have contributed to the development of pediatrics. Crookshank calls him the first epidemiologist of modern times. He came of good stock, his father, Nicolas, being celebrated both as a mathematician and as an architect. He studied in the University of Paris, and received his bachelor's degree in 1568 and his doctor's degree in 1570. From that time until his death in 1616, at the age of 78, he practiced in his native city.

As a teacher, de Baillou attained a reputation not only for imparting knowledge, but for his severity in examinations; this earned for him the title of "fleau des bacheliers." In 1580, he was made "doyen" by the faculty of Paris. Henry IV appointed him physician to the Dauphin, but he refused the appointment, saying that he preferred to be physician to "ses bourgeois de Paris."

De Baillou wrote much, but apparently nothing was published during his life time. He bequeathed his manuscripts to two physicians connected with his family, Jacques Thevart and Simon le Letier. The former edited many of his contributions, various volumes of which appeared from time to time, and finally Thevart issued them in a collected edition which first appeared in 1635 and went through many subsequent editions. In 1858, Prosper Yvaren translated the "Epidemics and Ephemerides" into French, and added an account of the life and works of de Baillou. His work ranks high. He was a good observer and a sound thinker, but his work followed Galen and the Arabians to its detriment, and the fashion of the day of mixing medicine with astrology led him to pay too much attention to the stars. But the fact remains that he was a follower of the Hippocratic method.

Whooping cough is such a distinctive disease that it could hardly have escaped description had it existed in ancient or medieval times. An epidemic appeared in Paris in 1578, and de Baillou has left a fine description of the disease. A short extract from it follows.

Summer Constitution, Anno Domini 1578

We have already previously spoken of the beginning of summer. At the end of the summer almost the same diseases flourished as before. The summer was

* Received for publication, July 16, 1928.

GVLIELMI

BALLONII

MEDICI PARISIENSIS

CELEBERRIMI,

EPIDEMIORVM

ET

EPHEMERIDVM

LIBRI DVO,

Studio & operâ M. IACOBI THEVART Medici Parisiensis, digesti, Scholiis aliquot illustrati, & in lucem primùm editi.

Ἀφόβως βιώσιν, ᾧ μὴ λανθάνῃ,
φθεγξάμενα πρόπαρ τι πικάσεις.

PARISIIS,

Apud IACOBVM QVESNEL, via Iacobæa, sub signe Cochleæ, & Columbarum.

M. DC. XL.

CVM PRIVILEGIO REGIS.

Title page of Ballonius.

glowing and burning hot. Boys four months old, ten months old a little older were attacked by fevers which carried countless off. Especially that common cough which is generally called quinta or quintana and which we have mentioned before. Its symptoms are serious. The lung is so irritated that, in its attempt by every effort to cast forth the cause of the trouble, it can neither admit breath nor easily give it forth again. The sick person seems to swell up and as if about to strangle holds its breath clinging in the midst of his jaws.

Why it is commonly called *quinta,* is not without doubt. Some think the word is a manufactured one through onomatopoiea, from the sound and the noise which those so coughing emit. Some do not seek its source hence, but think that the cough is called *quintana* in Latin because it recurs at fixed hours—a fact which experience proves to be true. For they are free from this annoyance of coughing sometimes for the space of four or five hours, then the paroxysm of coughing returns, sometimes so annoying that the blood gushes out through the nostrils and the mouth by violence. Very frequently the belly happens to be upset. I have not yet read any author who writes about this cough.

And they doubt whether it is from the head or from the body of the lung itself or from another source that the serum or ichor or whey or bestial distillation is wont to flow. It seems to be from the lung itself. For we have seen many so coughing, by whom after a fruitless attempt semiputrid matter has been ejected in an unbelievable quantity, so that it is probable that this matter resident and collected there is the cause of that cough. To others it seems to be from the head itself, as if liquefied by a sort of "melting" as Hippocrates says.

News and Comment

UNIVERSITY NEWS

Appointment of Dr. Weill-Halle.—Dr. B. Weill-Halle has been made head of the new School of Child Welfare established in the faculty of the University of Paris.

Appointment of Dr. Sedaillan.—Dr. Paul Sedaillan has been made "chef de clinique" of pediatrics in the faculty of the University of Lyons.

REPORT OF COMMISSION ON MEDICAL EDUCATION

The Third Report of the Commission on Medical Education is now available to subscribers of this journal gratis. Copies may be obtained from Willard C. Rappleye, M.D., Director of Study, 215 Whitney Ave., New Haven, Conn.

NEW SANATORIUM IN CHICAGO

A sanatorium is to be erected in Jackson Park on the site of the old World's Fair building, La Rabida, to be known as the Jackson Park Sanatorium and Day Nursery.

NATIONAL FELLOWSHIPS FOR RESEARCH IN CHILD DEVELOPMENT

Persons of either sex who are residents of the United States or Canada and who possess a Doctor's degree in one of the basic sciences or in medicine are eligible. In addition, the candidate must present tangible evidence of ability in research. Fellowships are open for study only in the United States or Canada. Fellowships carry a stipend of $1,800 a year and upward, varying with individual requirements. For further information write to Mervin A. Durea, Executive Secretary, Committee on Child Development, National Research Council, B and 21st Streets, Washington, D. C.

CONGRESS OF PAN-AMERICAN MEDICAL ASSOCIATION

The next congress of the Pan-American Medical Association will be held in Havana, Cuba, from Dec. 29, 1928, to Jan. 3, 1929.

Dr. William J. Mayo will give the oration on surgery and Dr. Lewellys Barker of Johns Hopkins University, the oration on medicine. Papers will be read in both Spanish and English.

APPOINTMENT OF DR. BRADLEY TO MAYO FOUNDATION

Dr. John W. Bradley of Wichita Falls, Texas, has been made a fellow in pediatrics at the Mayo Foundation.

CHILD HEALTH PROGRAM IN NEW JERSEY

Three hundred and fifty communities in New Jersey are carrying on a continuous child health program under the state department of health. This consists of visits to expectant mothers and to mothers of infants and older children. In the preschool clinics, 2,392 children were immunized against diphtheria, and more than 9,000 Schick tests and immunization tests were made among school children in the communities where these nurses are employed.

Abstracts from Current Literature

Pathology, Bacteriology and Biochemistry

SODIUM THIOSULPHATE: A STUDY OF THE TOXICITY AND CHEMICAL CHANGES IN THE BLOOD; INTRAVENOUS ADMINISTRATION. SAMUEL GOLDBLATT and CHARLES C. DENNIS, Am. J. Syph. **12**:369 (July) 1928.

The authors have made a study of the toxicity of sodium thiosulphate when used intravenously in animals. They find that the ordinary common, pure thiosulphate produces convulsions and sometimes death in experimental animals, if given in large doses, particularly if given rapidly and in concentrated solution. The drug is less toxic if given slowly and in dilute solution.

They find that pure sodium thiosulphate, which has been precipitated from an aqueous solution by alcohol, is entirely innocuous.

McBRIDE, Sioux City, Iowa.

THE DEVELOPMENT OF HUMAN MOTILITY AND MOTOR DISTURBANCES. G. SCHALTENBRAND, Arch. Neurol. & Psychiat. **20**:720 (Oct.) 1928.

During the development of human motility, some peculiar reflexes appear and later disappear. A number of them which exist during the second half of the first year of life are similar to reflexes of four-legged animals. Under pathologic conditions of the brain, all the primitive reflexes of childhood may reappear or may be preserved for an abnormally long time. Thus, one observes tonic neck reflexes in the limbs and a kind of Moro reflex in the decerebrate condition. In other patients with disease of the brain, a "quadrupedal syndrome" may appear with a positive neck righting reflex and with the primitive manner of rising from the floor to a standing position.

SANFORD, Chicago.

SUGGESTIONS AS TO THE CAUSE OF IMMUNITY FOLLOWING AN ATTACK OF ONE OF THE ACUTE INFECTIOUS DISEASES. FERDINAND HERB, M. J. & Rec. **126**:185 (Feb. 15) 1928.

The killing of pathogenic organisms within the body is brought about by defensive ferments which are the products of the cells. The ability of these cells to set free these ferments is only acquired after engulfing specific antigen in the form of specific organisms. In the first injection, some time elapses before this defense is set up; this period is known as incubation. In later injections, this defense is made immediately and the invading organisms are killed on settling. This is known as immunity. This immunity is gradually lost again. Artificial immunity may be kept up by the injection of the specific antigen at proper intervals. This continued supply of specific antigen keeps up the training of the cells and with it immunity as a consequence. Again, the preservation of the specific antigen in lesions and development of scar formation is fully substantiated by clinical observation. For example, the pus in the pustules of smallpox and the scales in scarlet fever are infectious, and it is highly probable that the specific antigen may be enclosed in the resulting scars and give up to the blood stream the infinitesimal quantity that is needed to sustain immunity. Deposits of specific antigen at favorable places in the body are probably the cause of the immunity which frequently follows an attack of one of the acute infectious fevers.

WILLIAMSON, New Orleans.

TREATMENT OF PARATHYROID TETANY WITH COD LIVER OIL AND YEAST. JOHN C. BROUGHER, Northwest Med. **27**:329 (July) 1928.

Finding that the administration of cod liver oil and yeast to parathyroidectomized dogs delayed the onset and lessened the severity of tetany, Brougher applied this form of therapy in patients becoming tetanic following thyroid lobectomy. Two patients were relieved of symptoms and hypocalcemia. Two other patients were relieved by cod liver oil alone.

SCOTT, Philadelphia.

THE ANTISCORBUTIC FRACTION OF LEMON JUICE. EDWARD HOYLE and SYLVESTER S. ZILVA, Biochem. J. **21**:1121, 1927.

The concentrated antiscorbutic fraction from lemon juice does not contain any manganese but contains traces of iron, phosphorus and sulphur. These elements of the active fraction behave on dialysis like the active principle.

THE EFFECTS OF COD LIVER OIL ON THE CALCIUM AND PHOSPHORUS METABOLISM OF THE LACTATING ANIMAL. DOUGLAS HARVEY, Biochem. J. **21**:1268, 1927.

The feeding of cod liver oil to goats improved the balance of calcium by reducing the amount excreted in the feces. The effects on phosphorus excretion were variable. In the case of animals in late lactation, the percentage and total amounts of calcium in the milk were increased by feeding cod liver oil. The amount of iodine in the milk was increased by feeding either cod liver oil or potassium iodide. The fat content of the milk did not show definite changes as a result of feeding cod liver oil. In a single experiment in which cod liver oil was replaced by olive oil plus an equivalent amount of iodine as potassium iodide, the effects of the former were not reproduced.

KUGELMASS, New York.

NITROGEN BALANCE AND C:N RATIO IN THE URINE IN EXPERIMENTAL SCURVY UNCOMPLICATED BY STARVATION. N. JARUSSOWA, Biochem. Ztschr. **198**:128 (July 19) 1928.

Jarussowa produced scurvy in guinea-pigs but prevented the occurrence of starvation by careful feeding. Over a period of several weeks, the nitrogen balance gradually became slightly negative. Only during the last week, when signs of starvation did appear, was there a large negative nitrogen balance. The variation of the nitrogen excretion in the urine was insignificant. The author feels that there is no evidence of increased endogenous protein destruction in her experiments.

M. B. BRAHDY, New York.

THE ANEMIA OF RICKETS. THEOPHIL BAUMAN, Monatschr. f. Kinderh. **39**:193, 1928.

The writer agrees with a host of previous observers that patients with rickets can be cured by either direct or indirect irradiation, even when they are kept exclusively on a milk diet. Direct irradiation consists of daily treatment with an ultraviolet ray lamp for from ten to twenty minutes. In indirect irradiation, milk, cholesterin, or ergosterin is treated with the ultraviolet ray, before being offered to the patient. All these forms of treatment cause a specific cure in from four to eight weeks.

Although the patient seems absolutely cured of the rickets, one symptom still remains, namely, the anemia. The author concludes that the anemia, therefore, is a symptom associated with the rickets rather than an integral part of it. The failure of the condition to respond to fruits proves that it is not the result of scurvy. Anemia can be avoided or the patient cured of it by a diet rich in vegetables or in metallic iron. In other words, the anemia accompanying rickets is due to improper diet, deficient in iron.

SALT FEVER OR SALT HYPERTHERMIA. DESIDER OROSZ, Monatschr. f. Kinderh. **39**:249, 1928.

By an experiment in which he produced a salt fever and found that antipyrin failed to reduce the temperature, the author believes that he has strengthened the theory of salt hyperthermia. The increase in temperature is due to a specific salt reaction.

INVESTIGATIONS ON THE ABSORPTION OF WATER INJECTED SUBCUTANEOUSLY. LUDWIG LEONHARDT, Monatschr. f. Kinderh. **39**:292, 1928.

Using the test of McClure and Aldrich, the writer determined the effect of age on the speed of water absorption. He found the age of the child to be an important factor. In nurslings, the average time was twenty-nine minutes, in small children thirty-four minutes and in school children fifty-two minutes. With increasing age there was a definite increase in the time of absorption. He attributes this fact to three factors: (*a*) The capillary network of the young child carries relatively more blood than that of the older child and so facilitates absorption. (*b*) The younger the child, the greater is the water binding property of the tissues. (*c*) The scanty development of the elastic tissue in infancy aids in the escape of fluid from the tissues.

GERSTLEY, Chicago.

THE ANTIRACHITIC ACTIVITY OF MILK IRRADIATED IN AN ATMOSPHERE OF CARBONIC ACID. K. SCHEER and P. ROSENTHAL, Ztschr. f. Kinderh. **44**: 235 (Oct.) 1927.

If fresh milk is exposed to ultraviolet light in an atmosphere of carbonic acid, it does not acquire an unpleasant smell or taste and is well taken by infants. Such milk protects infants completely against rickets, and in daily doses of from 300 to 500 cc. cures those with florid rickets in from four to six weeks.

THE TREATMENT FOR RUMINATION IN INFANTS. W. MANSBACHER, Ztschr. f. Kinderh. **44**:277 (Oct.) 1927.

In cases or rumination, a porridge with little if any milk is better than a porridge less firm but rich in milk. Mansbacher successfully fed 400 Gm. of potato soup plus 200 Gm. of whole milk fortified with 10 per cent butter, 10 per cent sugar and 10 per cent plasmon (a solution of casein in sodium bicarbonate) to three infants with habitual vomiting, aged, respectively, 8 months, 4 months and 2 years and 3 months. Later, the infants took egg, meat, bread and cottage cheese and tolerated them well. Vomiting is caused reflexly by the feeling of tension in the wall of the stomach. This disappears on the adoption of a diet of thick porridge, because with the setting in of perisystole, which is stimulated by thick food, the tonus of the stomach increases and the feeling of tension diminishes.

IRRADIATED ERGOSTEROL: THE INDIRECT LIGHT THERAPY OF RACHITIC DISEASES OF THE BONES IN CHILDREN, ADULTS AND ANIMALS. A. HOTTINGER, Ztschr. f. Kinderh. **44**:282 (Oct.) 1927.

Reference is made to contradictory results of research up to the present time on the antirachitic activity of irradiated cholesterin. The work of Heilbron, Pohl and Windaus on the absorption spectrum of irradiated and nonirradiated cholesterin was tested and confirmed; the results of the researches of Pohl, Windaus, Hess and Rosenheim on the absorption spectrum of ergosterin before and after irradiation with ultraviolet light and on its antirachitic activity were likewise studied. After a definite period of irradiation, in pure ergosterin a biologic optimum antirachitic product, 1,000,000,000 Gm. of which protected rats from rickets, arose. To the biologic optimum there corresponded a definite change in the spectrum and the abolition of the power of precipitation of ergosterol by a digitalis preparation. In experiments on dogs exhibiting spontaneous rickets and rickets produced

experimentally, irradiated ergosterin was especially active; in an astonishing manner, many analogies of rickets in human beings were shown, with reference to pathogenesis, clinical picture, the blood chemistry and pathologic histology. Healing occurred in children with florid rickets in from four to six weeks with the use of irradiated ergosterin, the ordinary dose of which was 1 mg., and in old, inveterate cases, from 2 to 3 mg. As a prophylaxis in premature infants weighing more than 2,000 Gm., the use of irradiated ergosterol was successful, although it could not protect premature infants of less weight against mild craniotabes, even in doses of 3 mg. a day. An infant with severe secondary dyspepsia who could not tolerate irradiated ergosterol or its vehicle, olive oil, was cured with Ravix, irradiated Swiss dried milk.

A man, aged 25, with chronic, late rickets and manifest tetany, was so much improved by the administration of irradiated ergosterol that in a few weeks the tetany became latent, the ossification almost normal and a clinical cure resulted; that is, the recovery of normal function of the bone. In one early and two severe forms of chronic osteomalacia, in which fractures and paralysis were present, the condition healed completely in a relatively short time under the influence of direct and indirect light therapy (Ravix and irradiated ergosterol). In patients with late rickets and tetany, the same mineral values were found in the serum as in those with infantile tetany and rickets. Strongly increased values after the determination of blood calcium were pathognomonic of osteomalacia. The doses in adults consisted of 5 mg. of irradiated ergosterol daily. The rickets in adults, however, necessitated a longer time for complete healing, and residual symptoms in osteomalacia occurred during convalescence after the therapy ceased. In the clinical picture of these diseases of the bones in adults, the sign of the flexibility of the tibia or pain on bending the lower leg was of real significance.

THE SUGAR BUILDING VALUE OF VEGETABLES IN THE DIET OF DIABETIC PERSONS. R. WAGNER and J. WARKANY, Ztschr. f. Kinderh. **44**:322 (Oct.) 1927.

An attempt was made with a biologic method to evaluate the carbohydrate content in vegetables used in the treatment for diabetes. The authors watched the blood sugar curve of a diabetic child, traced for periods of four hours, after the consumption of a definite quantity, from 10 to 20 Gm., of a white flour roll; then the effect of vegetable equivalents on the blood sugar of the same patient were compared. Kohlrabi, white cabbage, head lettuce and string beans were evaluated too highly by chemical analysis; according to the biologic method, their value must be reduced. Mushrooms and other fresh fungi were undervalued by chemical analysis; according to biologic test, their value must be raised. The values in the other vegetables studied agreed with the results obtained by chemical analysis, particularly because the equivalent values, hitherto, have been rounded off purposely, since allowance had been made for vegetables containing other carbohydrate than starch and sugar; for example, pentose, a carbohydrate which does not burden the metabolic process of diabetic persons.

STUDIES IN RICKETS: III. HEXOSEMONOPHOSPHATASE. O. JÄGER, Ztschr. f. Kinderh. **44**:358 (Oct.) 1927.

Hexosemonophosphatase is found in small quantities in the following body fluids of man and animals: the cerebrospinal fluid, intestinal juice, urine and, in the greatest amount, in the blood serum of infants. Of the organs of rats studied, a preparation of bones and kidneys split hexosemonophosphatase most and one of liver and muscle the least. The ability of this ferment to cause cleavage is greatly dependent on the hydrogen ion concentration the optimum of which lies between 7.5 and 8 in the blood serum, outside of the physiologic normal, and therefore cannot be completely unfolded in the living organism, whether healthy or rachitic. Cleavage in the serum diminished quickly in man after the first year, reached its lowest value at about the age of 25 years and increased again with age. A direct

and exclusive relation of cleavage with the process of ossification does not therefore exist; nor is there a direct relation to calcification, because the cleavage in rickets does not deviate from the normal. Under pathologic conditions, older children may develop an ability to cause cleavage corresponding to that in the infant, as was the case in a child aged 10 years, suffering from arachnodactylia. The reverse, however, may happen, as for example, in an infant, aged 6 months, with untreated myxedema, there was a diminished ability to cause cleavage, corresponding to that in older children. A direct and exclusive relation of cleavage with the calcium or phosphorus content of the serum, moreover, does not exist. This is shown, on the one hand, by the fact that in different calcium and phosphorus contents, whether normal, rachitic or indicative of tetany, the splitting effect is the same; on the other hand, at middle age or older, with the same phosphorus content, distinct differences occur. Views based on the meaning of phosphatase appear to the investigators to depend on the detection of the chemical nature and quantity of the substrates (phosphate esters). Only from these can it be determined whether, for example, differences in cleavage are to be regarded as etiologic agents or as secondary, perhaps regulating, phenomena.

THE SIGNIFICANCE OF CONGENITAL OSTEOPOROSIS FOR THE ORIGIN OF RICKETS. HANS ABELS and DORA KARPLUS, Ztschr. f. Kinderh. **44**:365 (Oct.) 1927.

An apparently irreconcilable conflict has come about as to whether congenital soft places in the skull are to be thought of pathologically and anatomically as nonrachitic, since they are different from rachitic craniotabes in their localization and time of appearance. On the other hand, close clinical relations between both processes have been confirmed. Rickets frequently develop, for example, from congenital alterations in the bones, and these alterations vary in intensity according to the time of year and whether the mother's environment is urban or rural. The early work of Abel established the fact of the geographic distribution of congenital soft places, which were localized and always confined to the roof of the skull, and the distinction in space and time between this anomaly and the later craniotabes. He based his conclusion on mechanical forces which disturb ossification, such as contact with the maternal pelvis, operating with a certain constitutional inferiority. This inferiority expresses itself best in children by localized soft places as well as by other signs of delayed ossification, such as wide sutures and fontanels, soft edges of the sutures, a particular form of head at the end of gestation, and measurements of weight and length below the average. The congenital soft places that arise on the basis of constitutional inferiority disappear in a short time after the cessation of active intra-uterine pressure. In their places, because of postnatal mechanical forces, other localized craniotabes-like soft places develop, which in the early months apparently and really have an osteoporotic character. At least, other rachitic symptoms in young infants with craniotabes have not been definitely established, even with the new methods of research. On the other hand, the special tendency of constitutional inferiority to lead to later rachitis could be demonstrated by the fact that children, who had shown at birth definite soft places in the skull, were found affected with rickets at the age of 4 months, almost without exception, while infants born with a hard skull, and studied in the same space of time, remained almost completely free from rickets. This tendency to the development of rickets is found in newly born infants without soft places in the skull but with wide, even if firm bordered, fontanels and sutures. Congenital lack of ossification or hypoplastic conditions are therefore looked on, in the usual form of appearance, not as physiologic but rather as a prerachitic osteoporosis. When the inferiority appears in the congenital osteoporotic change of the bone system it may be the result, at least partially, of harmful nutritional influences through several generations of the mother's family. The craniotabetic changes caused by osteoporotic processes in young babies challenge therapeutic influence, especially to ultraviolet light, and permit the preventive treatment for rickets.

EMERSON, Boston.

Nutrition

VITAMINS A AND D OF SPINACH. STANLEY G. WILLIMOTT and FRANK WOKES, Biochem. J. **21**:887, 1927.

An acetone-ether extract of dried spring spinach has been prepared more than 200 times as concentrated as the fresh leaves and practically free from mineral matter and oxidizing enzymes. The extract was a potent and stable source of vitamin A in that daily doses of 25 mg. secured complete freedom from xerophthalmia and induced satisfactory though slightly subnormal growth in rats. The extract, when fed at this level, does not appear to contain significant amounts of vitamin D.

EXPERIMENTS ON NUTRITION: BALANCE OF FOOD BY VITAMIN B. ROBERT H. A. PLIMMER, JOHN L. ROSEDALE and WILLIAM H. RAYMOND, Biochem. J. **21**:913, 1927.

Protein, fat and carbohydrate in the diet need balancing by vitamin B (B1 plus B2). The quantity of dried yeast, which carries the vitamin B required, can be represented by $\frac{\text{dried yeast}}{\text{calories}} = \frac{1}{40}$ to $\frac{1}{60}$ or from 6 to 10 per cent in a food not containing vitamin B in the case of chickens. The ratio is about $\frac{1}{80}$, or 4 per cent, of the food in the case of adult pigeons and $\frac{1}{100}$, or 2 per cent, in the case of adult rats. Eight per cent of marmite corresponded to 4 per cent of dried yeast as tested on pigeons. Samples of yeast extract have been found to vary considerably in their vitamin B content. Young animals require more vitamin B than adult animals. It is therefore suggested that vitamin B is a constituent of the nucleus of the cell and is required for growth and for replacement of wear and tear. Various pathologic conditions, obviously affecting the intestines and heart, are noticed on diets containing too little, or a shortage of, vitamin B. These symptoms have been described as occurring in the early stages of beriberi. On a shortage of vitamin B, these early symptoms become a chronic condition of ill health.

GROWTH AND REPRODUCTION ON SYNTHETIC DIETS. GLADYS A. HARTWELL, Biochem. J. **21**:1076, 1927.

Three generations of rats have been reared on a synthetic diet of butter, caseinogen, potato starch, salt mixture, marmite and distilled water. The use of cod liver oil instead of butter in this synthetic diet produces less good growth and causes sterility. Synthetic diets are described which produce good growth in young rats, but cause inability of the young to be born and consequent death of the doe. Further evidence is given that the dietary requirements of the rat vary at different phases of its existence.

THE PHYSIOLOGICAL RÔLE OF VITAMIN B. THE RELATION OF INANITION TO VITAMIN B. DEFICIENCY IN PIGEONS. GUY F. MARRIAN, LESLIE C. BAKER, JACK C. DRUMMOND and HERBERT WOOLLARD, Biochem. J. **21**:1336, 1927.

The administration of extracts rich in vitamin B does not prevent the hypertrophy of the suprarenal glands in pigeons that are deprived of food. This is contrary to the conclusion of Beznak. In most cases the epinephrine content of the glands of starving pigeons, whether receiving vitamin B or not, is increased proportionately to the hypertrophy. This tends to confirm the opinion of McCarrison that the hypertrophy is medullary. A slight but definite hyperglycemia is observed in pigeons during most of the course of inanition. It is followed by a marked fall in the amount of blood sugar coincident with the premortal fall in body temperature. The administration of extracts rich in vitamin B has no effect on the blood sugar levels of such birds. Nervous symptoms similar to those observed in pigeons suffering from deficiency in vitamin B were observed in a

number of starving birds. The incidence of such symptoms was not increased by the daily administration of large volumes of water. These convulsions cannot be due to a deficiency in vitamin B resulting from starvation, since several cases were observed in birds receiving daily administration of vitamin B. The symptoms observed in starving birds always occurred during the period just before death when body temperature and blood sugar were much reduced. This is in contrast to the established fact that nervous manifestations in pigeons nourished on rations deficient in vitamin B usually appear when the temperature is slightly reduced and the blood sugar level is, if anything, above normal. By forcibly feeding pigeons on larger quantities of a diet deficient in vitamin B than they would voluntarily consume, the authors produced typical nervous symptoms of beriberi in about sixteen days, at a time when the loss of body weight was almost negligible. The suprarenal glands of the forcibly fed pigeons were hypertrophied to a considerable extent, although a corresponding increase of the epinephrine content was not observed. At present a satisfactory explanation of this is not forthcoming.

KUGELMASS, New York.

INFANT FEEDING. H. BROOKER MILLS, M. J. & Rec. **127:** concluded from p. 374 (April 18) 1928.

For all practical purposes the author advocates in the beginning a formula of acidified milk after which he uses a milk, water and sugar formula. Also he obtains a fair degree of success with the so-called egg yolk-orange juice mixture used so extensively by Hess and others. This is especially suited for institutions. The regular pasteurized milk was used in these formulas, but if only raw milk was obtainable, it was boiled before using. The proportions of egg yolk, orange juice, milk, water and sugar as well as the method of preparation of this formula, as well as that of acidified milk, are given in the paper. Carrot and spinach juice are commenced at the third month. Fruit juices of all fresh fruits are given at the fifth month to breast-fed infants, and the author places at the head of the list canned tomato juice. The juices are given in a bottle between feedings. The diet of an artificially fed infant should be changed every month. The bottle should be given for one year from the time it was begun. A child should not be made to eat when suffering from anorexia, but it should be taught to eat the food that is good for it.

In infants with pyloric stenosis, the proper diet consists of equal parts of thick cereal and mashed potatoes. All liquids should be stopped. Human milk is sometimes claimed to be the best form of milk in these cases, but the author has obtained better results from acidified milk when he tried a liquid diet.

WILLIAMSON, New Orleans.

RECENT WORK ON VITAMINS. R. H. A. PLIMMER, Practitioner **121:**9 (July) 1928.

Vitamins A and D.—The differentiation of the fat soluble vitamin A into two separate factors was the first stage in the recent work on rickets. The similar distribution and chemical and physical properties led to the assumption that the two were identical. Cod liver oil was shown by McCollum to contain two vitamins: vitamin A, the antixerophthalmic substance, and vitamin D, the antirachitic substance.

The discovery of ergosterol, its activation by ultraviolet light and the demonstration of its preventive action against rickets bring together the two opposing views of the causation of this disease. Two factors are necessary for its prevention. One is ergosterol in the food and the other is sunlight or ultraviolet rays. Sunlight on the body in the absence of ergosterol is valueless.

Foods may contain either ergosterol or vitamin D. Those containing vitamin D prevent rickets. Those containing ergosterol require irradiation or moderation of the animal.

Vitamin B.—The work on this vitamin has been chiefly on the quantitative side. It was found that the amount of vitamin B must have a definite relation to the food consumed, expressed as $\frac{\text{Vitamin-B}}{\text{Total food}} = \text{a constant}$, for an adult animal. This ratio, however, does not satisfy the needs of a young growing animal who needs more than the adult.

The amount of yeast used in baking bread is insufficient to supply enough vitamin B to balance the food. The common belief that vegetables contain vitamin B is erroneous.

A distinction should be made between absence and shortage of vitamin B. It is likely that many chronic ailments in man may be due to too little vitamin B. Efficient lactation is secured only by from 3 to 5 times the amount of vitamin D in the diet. Rheumatic conditions are possibly influenced by a shortage of vitamin B and also maternal mortality at childbirth. There is some evidence of the benefit of taking an extra amount of vitamin B and of the average diet having too little.

Vitamin B_2 or PP.—Goldberger called this substance PP or pellagra preventing substance. It is not the same as vitamin B, although they are commonly found in the same foodstuffs.

Vitamin C.—The least stable of the vitamins to heat is vitamin C. Investigations have been carried out with reference to its preservation. Fruits were found to retain their vitamin C if canned or concentrated in the absence of air. It is better not to rely entirely on canned fruits as a source of vitamin C.

The concentration of orange juice in vacuo without the loss of vitamin C is of value in Arctic expeditions. Certain milk powders have also been prepared with dried orange juice.

GELSTON, San Francisco.

THE OCCURRENCE OF CAFFEINE IN THE BREAST MILK AFTER DRINKING COFFEE. E. SCHILF and R. WOHINZ, Arch. f. Gynäk. **134**:201 (June) 1928.

Nursing mothers were given coffee containing a measured amount of caffeine —about 90 mg. a cup. Approximately 1 per cent of the amount taken was excreted in the breast milk. Daily large quantities of coffee may be harmful to the infant.

BRAHDY, New York.

KEFIR. KARL SVEHLA, Jahrb. f. Kinderh. **119**:263 (April) 1928.

Svehla writes an extensive article on kefir, its production, its properties and its uses. On the basis of his biologic and clinical investigations thus far, he remarks that he has been able to preserve his kefir fermented milk for six years. During this time it has still retained all of its desirable qualities. It has a pleasant taste and is not harmful to the organism.

By experiments on pigeons he has shown that kefir prevents symptoms of avitaminosis when fed with polished rice (which caused typical symptoms of avitaminosis in the control pigeons).

Kefir exerts a definite, but temporary, therapeutic effect on polyneuritis in pigeons.

The author considers kefir as an important element in the diet of children and adults and as an economic food which may be kept for a long time.

The kefir ferment is a symbiotic mixture of *Lactobacillus caucasicus* and the kefir yeast *(Torula kefir)*.

THE INFLUENCE OF THE FATS ON THE NUTRITIVE VALUE OF INFANT'S FOOD. F. THOENES, Jahrb. f. Kinderh. **120**:1 (May) 1928.

Thoenes gives a brief historical summary of the theories of artificial feeding with milk dilutions. He mentions Pirquet's point of view that fats may be administered in isodynamic amounts with regard to the carbohydrates without causing injury in the growing organism. In 1918, Czerny and Kleinschmidt popularized the "butter-flour" mixture.

The author attempted to study and compare the relative energy values of ordinary half-milk dilutions and carbohydrates with a diet rich in fats such as occurs in "butter-flour" mixture.

Close metabolic studies were made on seven children from 1 to 5 months of age. The energy quotient was determined for normal amounts of half-milk dilutions, butter-flour and mother's milk.

As a result of thorough and painstaking determinations, the author concludes that the energy quotient of Czerny-Kleinschmidt's "butter-flour" mixture is no higher than with half milk dilutions poor in fat content. Also, the fat in the "butter-flour" diet does not exert a specific dynamic action. In fact, the catabolism of all three diets mentioned was of equal degree. Calcium and phosphorus were less readily retained with "butter-flour" feeding. In the presence of infection and nutritional disturbances, there is a fat intolerance and thus a higher energy quotient in the use of "butter-flour" nourishment.

The author ascribes a large part of the error in the literature, however, to mistakes in determination of the energy content of the food. There are wide fluctuations in the energy content of food, and the author advises personal analysis of the food used in the experiment instead of resort to the tables in the literature.

CONCENTRATED RICE-WATER AS THERAPEUTIC AGENT. A. J. FELDMAN, Jahrb. f. Kinderh. **120**:72 (May) 1928.

Feldman notes that the course and prognosis of acute diarrheal disturbances of infancy have been greatly improved in recent years. The work of Czerny and Finkelstein is briefly mentioned. The dangers of undernourishment and excessive starvation periods in these conditions are particularly emphasized. Czerny has demonstrated the favorable effect of carbohydrates and water on the child with fever. On the basis of this work, Schiff introduced the use of Ringer's solution plus 15 per cent of grape sugar in the treatment for acute nutritional disturbances of children. Mayer showed that with the addition of carbohydrate and water the nitrogen loss was diminished. Further, it has been shown that acidosis and intoxication arise in these children with insufficient water intake. Products of intermediary metabolism rise in the blood.

The author considers the suggestion of Bessau (*Deutsche med. Wchnschr.* **15**:723, 1925) valuable. This consists in the use of concentrated rice water with the addition of from 2 to 5 per cent sugar in the treatment for gastro-intestinal disturbances of infancy. Bessau reported good results in seventy-nine cases. The author reports his results with sixteen infants suffering from fever and intoxication.

He finds that Bessau's therapy is an effective method of dealing with these disturbances and may be used as a readily assimilable nourishment directly after the hunger diet. The concentrated rice water favorably influences the phenomena of intoxication, lowers the temperature and improves the general condition. It hastens the coming of the reparation period. It alone, however, is insufficient for caloric needs and growth, and it is thus necessary to add water, albumin and carbohydrate.

THE RELATIONSHIP OF THE AMINES TO DYSPEPSIA AND INTOXICATION. H. RÖTHLER, Jahrb. f. Kinderh. **120**:162 (June) 1928.

Röthler writes that the literature in recent years has emphasized the occurrence of amines in the intestinal tract as a normal process. This is accomplished by *Bacillus coli* which has the ability to split albumin and peptones into amines. It is thought by Schiff and Kochmann that a secondary poisoning with amines may occur after a primary injury to the liver, thus interfering with its detoxicating function. In healthy infants, the large intestine has most of the amines. However, in the presence of acute nutritional disturbances or infections the formation of amines may go on in the small intestine.

When there is an increase in *B. coli* there is an increased formation of amines, and this process may extend into the small intestine.

The author found that in dyspepsia there is an increase in the amines from 100 to 1,000 times the normal. The work of Boyd is mentioned in which the portal blood from toxic infants was found to have a high toxicity.

The author also thinks it highly probable that an enterogenous poisoning with amines may occur without previous injury to the liver.

In conclusion, the author states that formation of amines occurs in the large bowel in normal infants and in dyspeptic infants also in the small intestine. In dyspepsia the formation of amines is considerably increased. In four of six cases of intoxication, an aminuria was observed. The possibility of a primary enterogenous amine poisoning is mentioned. The technic of determination of amines is thoroughly and critically described.

RENAL RICKETS AND RENAL DWARFISM. P. GYORGY, Jahrb. f. Kinderh. **120**:266 (July) 1928.

Gÿorgy observes that in the past two decades there have been reports in the literature of instances of marked inhibition of growth, general infantilism associated with more or less definitely rachitic changes in the bones as a result of renal disturbances. Goodhart (1872) was the first to describe the condition. Morley Fletcher (1911) was the first to correlate definitely the various rachitic manifestations and disturbances of growth with chronic nephritis.

There is an insidious onset with inhibition of growth or the more sudden occurrence of florid rickets with genu valgum as a common complication. For a long time the renal symptoms precede the changes in the bones; these are usually a marked thirst and polyuria, often misdiagnosed as diabetes insipidus. There is frequent hypertension. A diminution in renal function, delayed excretion of indigo-carmine and nitrogen retention in the blood serum occur. Headache, vomiting, ocular symptoms and drowsiness signify an impending uremia, the usual termination of the illness. Cure occurs rarely. Occasional associated phenomena are anemia, brown pigmentation of the skin and dry, bristly hair. Autopsy shows progressive fibrosis of the kidneys with cystic degeneration of the tubules. The kidneys are normally quite small. Fletcher is of the opinion that an ascending or descending infection of the genito-urinary tract is the cause of the condition. There have been seventy-eight instances of renal infantilism reported up to the present.

The author reports three cases of renal dwarfism with a chronic pyuria as a most conspicuous manifestation, associated with rachitic changes in the bones. Numerous roentgenograms showed characteristic osteoporosis in the long bones. Examination of the blood revealed hypocalcemia and hypophosphatemia. The author stresses the importance of Looser's "umbauzonen" areas of osteoporosis as demonstrated by x-ray examination of the long bones.

ARTHUR ABT, Chicago.

THE EFFECT OF A TRYPTOPHAN-POOR DIET. EMERICH SCHILL, Wien. Arch. f. inn. Med. **15**:547, 1928.

The author's experimental results show that food poor in tryptophan distinctly depresses metabolic functions in contrast to high protein feeding, notably with meat protein. The former rather than the latter diet is recommended for hyperthyroidism.

SCHLUTZ, Minneapolis.

DECLINE IN IMMUNITY AS A SYMPTOM DUE TO DEFICIENCY IN VITAMINS A AND C. C. E. BLOCH, Acta Paediat. **7**:61 (April) 1928.

Bloch has previously expressed the opinion that deficiency in vitamin A is clinically manifested not only by arrest of growth and xerophthalmia, but also by a decline in resistance to infection. In order to show that the last feature is a specific attribute of deficiency in vitamin A and not of all avitaminoses, he compares the morbidity of infections in a series of thirty-two patients with scurvy and eighty-

six with xerophthalmia drawn from comparable environmental sources. Of the former, less than 30 per cent showed some infection either on admission or during the stay in the hospital, whereas nearly 80 per cent of the latter showed infections.

SUGAR OR PROTEIN IN THE TREATMENT FOR INTOXICATION IN INFANTS. ARVO YLPPÖ, Acta Paediat. **7**:65 (April) 1928.

Ylppö takes exception to the statement of Schiff that in the treatment for alimentary intoxication the food should consist, at least during the first few days, exclusively of sugar solutions. On the contrary, he emphatically reiterates his belief that a diet rich in protein, because of its deterrent effect on the growth of organisms of the colon group, offers the best means of allowing the diseased intestine an interval of recuperation. He admits that the mortality of this condition is lower in German reports, but lays this to the fact that in Finland the bed capacity in hospitals is meager and that patients are often admitted only when in a dying condition.

SACCHAROSE TOLERANCE AND SACCHAROSURIA IN CHILDREN. O. UTTER, Acta Paediat. **7**:71 (April) 1928.

Utter studied saccharosuria in 130 tests on nineteen patients ranging in age from 1½ months to more than 10 years, by giving various amounts of cane sugar, calculated as grams per kilogram of body weight, in varying concentrations of solution. The total urinary output of sugar was seldom greater than 1 Gm., and as a maximum in one case reached 3 Gm. (2 per cent of the amount fed). Utter found that, with a constant amount of sugar given, saccharosuria occurred when the carbohydrate was given in concentrated solution, for example, 80 per cent, but did not occur when a lower concentration, such as 20 per cent, was used. Patients who had been accustomed to a saccharose-free diet, such as nurslings, might acquire an increasing tolerance for cane sugar by repetition of the tests. When sugar was given with egg, casein, or 10 per cent cream, the threshold of saccharosuria was raised; but it could be lowered by giving sodium bicarbonate by mouth either simultaneously with the sugar or an hour later. Soda has the opposite effect on glycosuria and hyperglycemia. In spite of the large doses of cane sugar, diarrhea was observed only twice and lasted for only one day, although the experiments were not interrupted. The children invariably throve during the tests.

ACIDOSIS IN INFANTS FED ON FORMULAS RICH IN EGG AND CASEIN. V. RANTASALO, Acta Paediat. **7**:83 (April) 1928.

By studying the urinary p_H and the output of ammonia, titratable acids and organic acids, Rantasalo endeavored to determine whether casein, egg white, egg yolk or whole egg added to the diet had an acidotic effect on the internal metabolism. He concluded that egg and especially egg yolk put a load on the acid-base regulating mechanism, but that the effect of casein is still in doubt.

MCINTOSH, Baltimore.

BREAST FEEDING AND THE CONDITION OF LIVING. M. GROMSKI, Opieka Nad Dzieckiem **6**:194, 1928.

The author has found that in his section of Poland the percentage of breast-fed infants decreased from 64 in 1922 to 50 in 1926. He blames chiefly the increased cost of food with which the increase in wages has not kept pace, and the changed economic conditions which take women from the homes and place them in factories. He suggests that adequate compensation be given mothers, married or unmarried, until the child has reached the twenty-sixth week.

LESLIE, Evanston.

VARIATIONS OF THE FERMENTS IN THE BLOOD AND THE GASTRIC JUICE, AND OF THE ACIDITY OF THE STOMACH IN INFANTS IN CONNECTION WITH FEEDING WITH BUTTERMILK AND CARBOHYDRATES. M. ZINGER, Pediatriya **11**:123, 1927.

The author studied the question of fermentation and acidity in connection with feeding buttermilk and carbohydrates to thirty-two children. He first studied the ferment indexes on infants with their usual food (mother's milk, diluted cow's milk and other foods); then the child was given buttermilk, and after eight or ten days the indexes were again studied. The reaction of the child to buttermilk and carbohydrates and his weight and general condition were considered. The children were from 12 days to 11 months old and were in various conditions of nutrition. The buttermilk was given with 2 per cent of flour and from 3 to 4 per cent of sugar. Children on mother's milk received one half or two thirds of their food in the form of buttermilk, and children on cow's milk, two thirds of the total amount in buttermilk. Blood was taken in the morning on an empty stomach. Gastric juice was taken forty or forty-five minutes after the test meal (from 120 to 150 cc. of 2 per cent rice water with 2 per cent of sugar).

The author's conclusions are as follows:

1. Buttermilk influences eutrophic and dystrophic children somewhat differently.

2. Buttermilk decreases the general acidity and the amount of free hydrochloric acid in the gastric juice in all cases, independently of the general conditions of nutrition.

3. In eutrophic children who have not yet received carbohydrates in their food, it gives an increase of the amylolytic index in the blood, but not in dystrophic children.

4. The lipase of the blood and gastric juice in both eutrophic and dystrophic children usually decreases.

5. Children with low acidity and fermenting capacity of the stomach do not tolerate buttermilk and do not show good results, and all their fermenting indexes are depressed.

6. There is a certain dependence between the state of nutrition of a child and the fermenting index. In malnutrition, the indexes decrease; with recovery, they increase.

7. Infection and functional disorders of the gastro-intestinal tract affect the fermenting indexes.

SEVERAC, Philadelphia.

Prenatal Conditions

CONGENITAL RADIOULNAR SYNOSTOSIS. JACOB GROSSMAN, M. J. & Rec. **127**:186 (Feb. 15) 1928.

Congenital radio-ulnar synostosis is not common. Heredity may play a rôle in some cases. The condition may be unilateral or bilateral. Two types are described: one in which the fusion is accompanied by dislocation of the head of the radius and one in which there is fusion of the radius and ulna alone. The radius is generally fixed in pronation. Most of the cases in childhood are discovered accidentally, as the disability caused by this condition is slight. Operative intervention may be instituted in either childhood or adult life. In practically every child operated on the condition has recurred. The author reports three cases in patients aged 4, 7 and 13 years, respectively, in all three of which he pursued a waiting policy.

A CASE OF INTRA-UTERINE FRACTURE OF THE TIBIA AND FIBULA. B. WHITCHURCH HOWELL, Proc. Roy. Soc. Med. **20**:1262 (May) 1928.

An infant, aged 5 months, sustained a fracture in utero. At 5 months malunion of the tibia and fibula with abduction and backward displacement of the

lower ends resulted in marked talipes calcaneovalgus and shortening. A suggested line of treatment is given in the report. The cause of the fracture might be from lack of amniotic fluid causing a true pressure-fracture. There was no history of injury to the mother before the birth of the infant, and instruments were not used. The report is accompanied by roentgenograms.

SWELLING IN THE REGION OF THE TENDO ACHILLIS. B. WHITCHURCH HOWELL, Proc. Roy. Soc. Med. **20**:1265 (May) 1928.

The patient, aged 13 years, had suffered from swelling in the region of the tendo achillis since birth. The swelling had been partially removed in 1920. X-ray examination showed a shadow in the region of the swelling, which was not obviously calcareous. The swelling was said to be increasing in size. Opinions were asked as to diagnosis and operative treatment.

WILLIAMSON, New Orleans.

THE ELECTRICAL EXCITABILITY OF THE FETAL MUSCULATURE. M. MINKOWSKI, Schweiz. Arch. f. Neurol. u. Psychiat. **22**:64, 1928.

The writer investigated the electrical excitability of the muscles of twenty fetuses, ranging in length from 3.5 to 35 cm., i. e., from the ages of 2 to 7 months. The specimens were examined promptly after delivery and kept at body temperature, since chilling in itself may change the reactions both quantitatively and qualitatively. Minkowski found that the fetal musculature responds to stimulation by both the galvanic and the faradic currents after the third month. The response to the faradic current is always tetanic and resembles that noted in the adult. The response to the galvanic stimulus, however, varies. There may be a lightning-like response, a somewhat prolonged response, without tetany, and, as is usually the case, a tetanic reaction which persists during the entire time the galvanic current is applied. The muscle may be excited on stimulation of the nerve trunk with the galvanic current relatively early in life, i. e., from the fourth month of fetal life. This is interesting, as the nerves are at this time still without a myelin sheath. The slow response to galvanic stimulation resembles the response seen in a muscle which has been subjected to asphyxia, cooling or injury to its motor nerve.

The facts that a myotetanic reaction to galvanic stimulation occurs in many fetal muscles, that this reaction occurs in muscles which are less excitable, and that it appears toward the end of the period of observation, suggest that in fetal muscle there is a more primitive and resistant form of direct aneural irritability. Von Frey found a cathodal closing tetanus almost regularly in frogs which had been kept at a temperature below 10 C. for a time. The contraction of smooth muscle to the electric current is also slow. The fetal tetanic reaction bears certain resemblances to the myotonic reaction of Thompson's disease. The continued contraction for the duration of the galvanic current, as well as the faradic current, is observed in fetal muscle, but the persistence of the contraction after interruption of the current is not seen here as it is in Thompson's disease.

The question whether this response bears any relationship to the anatomic structure of the muscle naturally presents itself. Weiss found a relationship between the histologic development and the functional character of fetal muscle in the frog and axolotle. He arrived at the conclusion that embryonic muscle, because it has either no or very little differentiated myofibrillary substance and a predominance of sarcoplasm, has a contraction which is tonic in nature. It is only with the development of myofibrils that short twitches become possible, and that the amplitude of the twitch rises with the intensity of the stimulus.

WOLTMAN, Rochester, Minn.

THE PHYSICAL AND PSYCHIC DEVELOPMENT OF PREMATURE INFANTS. SIEGFRIED LEVY, Jahrb. f. Kinderh. **121**:41 (Aug.) 1928.

The material studied by Levy includes all premature infants weighing less than 2,500 Gm. during the years 1918-1926. There were 403 children in the entire

group. The mortality was 53.5 per cent. The cause of prematurity was determined in 30 per cent of the cases. In 14.81 per cent twins were the cause. Syphilis occurred in 3.2 per cent. In 22 per cent, the mother had had either a previous premature infant or a miscarriage. A relationship was not noted between the age or the number of previous deliveries of the mother and the incidence of prematurity. The third week of life seemed to be the critical period as far as mortality was concerned. The frequency of skin disturbances and nutritional disturbances is emphasized. Infections in premature infants are of more serious prognostic significance than in normal new-born infants. The early occurrence of rickets in premature infants is noted. Static development is slow and delayed. Development as to height approaches the normal much sooner than development in weight, which remains even at 8 or 9 years of age. The tables show that with increasing age there is an increase in the number of infections which, however, does not seem more prevalent than in the normal new-born infant.

In thirty-two of seventy-six cases there was a definite diastasis recti, the remains of a previous umbilical hernia. Cryptorchidism occurred in 50 per cent of the boys. Dentition was delayed for from six to twelve months. Signs of rickets were found in all but two instances. There was a delay in the ossification centers of the bones in 20 per cent of the children.

Examination of the blood showed a greater delay in the rise of hemoglobin than in the increase of erythrocytes. Differential examination of the blood showed a delay in the neutrophil increase.

A particularly marked tendency to mental deficiency was not observed.

ARTHUR ABT, Chicago.

Diseases of the New-Born

INTRACRANIAL HEMORRHAGE IN THE NEWLY BORN: A STUDY OF ITS INCIDENCE, CAUSES, RELATION TO BREECH EXTRACTIONS, AND DIAGNOSIS. THEODORE C. GREENE, Boston M. & S. J. **197**:1302 (Jan. 12) 1928.

The author's summary is: 1. Intracranial hemorrhage is the most frequent cause of death in the newly born and was found in 55 of 177 consecutive autopsies performed at the Boston Lying-in-Hospital. 2. The most important cause of intracranial hemorrhage is injury to the child's head during delivery, especially if force is applied suddenly. 3. Hemorrhagic disease is also an important factor in producing intracranial hemorrhage. 4. Intracranial hemorrhage occurs most often in primiparous and operative deliveries, and especially in connection with breech extractions. 5. In this clinic, however, only 6 instances of intracranial hemorrhage occurred in 258 consecutive breech extractions (not preceded by version). 6. Intracranial hemorrhage occurs in a number of simple, uncomplicated breech deliveries which are not considered difficult at the time. This ever present possibility emphasizes the folly of the routine use of version and breech extraction for all deliveries. 7. The diagnosis of intracranial hemorrhage in the newly born is usually definite, and the outcome is not always fatal.

INTRACRANIAL HEMORRHAGE OF THE NEW-BORN: ITS RELATION TO THE HEMORRHAGIC DIATHESIS. B. P. BURPEE, Boston M. & S. J. **197**:1449 (Feb. 2) 1928.

While infant mortality in general has decreased, intracranial hemorrhage in new-born infants still accounts for about half of the deaths occurring during the first two weeks of life. Blood will be found in the spinal fluid of about 10 per cent of all new-born infants, but not in all infants suffering from intracranial hemorrhage. Intracranial hemorrhage due to trauma and hemorrhagic disease of the new-born are two separate conditions. Epidural and subarachnoid hemorrhages are common but usually without symptoms; dural or subdural hemorrhages produce serious or fatal results. They may be supratentorial, infratentorial or mixed, and may more rarely occur into the ventricles or the brain substance.

Intracranial hemorrhage may be caused by trauma, or by the predisposing factors, such as prematurity, syphilis, maternal toxemia, asphyxia and hemorrhagic diathesis. The importance of trauma as a factor is established by the fact that the death rate from intracranial hemorrhage is higher in the firstborn, and in male infants over the average size. An important factor is the too rapid compression of the head, whether due to passage through a too narrow birth canal, to the improper use of forceps, to the use of too powerful doses of solution of pituitary (more than 4 minims [0.24 cc.]), or to breech deliveries.

The following treatment is advised: the injection of at least 20 cc. of whole blood intramuscularly (the author believes blood transfusion harmful); lumbar puncture, to relieve intracranial pressure, repeated every six, twelve or twenty-four hours according to the symptoms, and measures to prevent dehydration.

GENGENBACH, Denver.

AN UNUSUAL INFECTION IN A NEW-BORN INFANT. KOLN SCHLESINGER, Monatschr. f. Kinderh. **39**:281, 1928.

An infant, aged 2 days, developed a purulent infection of the salivary gland, a phlegmon involving the floor of the mouth, and septicemia which resulted in death. Postmortem examination did not reveal the cause. The author believes that the child was congenitally infected, and that the mother was able to overcome the infection.

GERSTLEY, Chicago.

CHANGES IN THE LUNGS OF PREMATURE AND FULL-TERM INFANTS, SECONDARY TO THE ASPIRATION OF AMNIOTIC FLUID. HELGA HINTNER, Ztschr. f. Kinderh. **44**:483 (Nov.) 1927.

With the object of finding the cause of death of premature and full-term infants, Hintner studied fourteen cases. The aspiration of amniotic fluid was not constantly followed by demonstrable changes, but purulent inflammation and the formation of granulation tissue frequently happened and occasionally caused death. One case reported, remarkable also for a hemicrania, showed granulation tissue and small abscesses in both lungs. Whether the malformation of the brain was of significance etiologically could not be decided.

THE ETIOLOGIC OVERVALUATION OF BIRTH TRAUMA. LOTTE LANDÉ, Ztschr. f. Kinderh. **44**:535 (Nov.) 1927.

Landé warns against overvaluation of birth trauma as an etiologic agent and reports two cases which were thought to be caused by birth trauma but which showed, respectively, microcephaly, focal sclerosis and a small right cerebral hemisphere with a dilated right ventricle. Destructive processes due to different causes can call forth the same symptoms when the same important brain centers are attacked, and extensive alternations in unimportant centers may pass unnoticed. Many patients who die under fulminating clinical conditions show hardly any anatomic change in the brain, while extensive destruction may occur which over a course of years gives only slight manifestations.

EMERSON, Boston.

Acute Infections

THE CONQUEST OF COMMUNICABLE DISEASES WITH SERUMS AND VACCINES. RALPH OAKLEY CLOCK, M. J. & Rec. **127**:289 (March 21) 1928.

1. Diphtheria.—The essential point in the antitoxin treatment for diphtheria is to give a sufficient dose to neutralize all of the toxin in the blood at the earliest possible moment. One large dose given early is far more efficacious than the same amount given in divided doses. Woody at the Philadelphia Hospital for Contagious Disease recommends that not any person with diphtheria, how-

ever mild the disease, should receive less than 10,000 units and more if the antitoxin is not given on the first day and that from 20,000 to 40,000 units should be given in severe forms in which treatment is begun late or in malignant forms. Prevention with toxin antitoxin is then discussed and statistics quoted to show how the cities have reduced their death rate as a result of an extensive campaign of immunization against the disease with toxin antitoxin.

2. Scarlet Fever.—Scarlet fever is transmitted only through air borne droplets of saliva or nasal discharges or by contact with articles soiled with discharge and not by the scales from the skin, as previously believed. Serum treatment, when it is indicated, and the dose, results and prophylaxis are then discussed.

3. Erysipelas.—Almost every kind of treatment has been used for erysipelas, most of it based on the application of local remedies, but the most recent treatment is that with antitoxin introduced by Birkhaug. The antitoxin treatment for erysipelas marks an advance, the results of which are commensurate with those obtained in the treatment for diphtheria. The dose of antitoxin must be determined for each case; the duration of the disease before treatment has been started, the patient's resistance, the virulence of the infection and the part of the body involved must be considered. The dose is repeated every twenty-four hours until the blush disappears and the temperature becomes normal.

4. Pneumonia.—The serum treatment for pneumonia was used for years, until the weight of clinical opinion caused its abandonment as of no value. In 1910, it was discovered that there were several types of pneumococci. These types are easily distinguished by laboratory tests. The gain to therapeutics of this classification is due to the fact that an active serum has been produced against only one type of pneumococcus which is known as type 1. Hence, to treat persons with pneumonia rationally and scientifically with serum, the disease must be caused by type 1 pneumococcus. The serum should be administered intravenously in an initial dose of 100 cc. and repeated every eight hours until the temperature falls.

5. Serum Reactions.—In approximately 60 per cent of patients treated with serum, serum sickness develops, and in 40 per cent a thermal reaction takes place. About one in every 20,000 primary injections of serum is followed by an anaphylactic reaction. The eye test is explained, and treatment for prevention of the foregoing reactions is given.

WILLIAMSON, New Orleans.

SOME PROBLEMS OF RHEUMATIC INFECTIONS. D. M. LYON and A. R. GILCHRIST. Tr. M.-Chir. Soc., Edinburgh M. J. **35**:145, 1928.

Whether *Streptococcus viridans* or some other type is the causative organism of rheumatic infections, the pathogenic condition is regarded by Lyon as of relatively low infectivity. Even if there is a positive family history in from 20 to 70 per cent of cases, this cannot be accepted as proof of a hereditary predisposition, as exposure to similar environments and direct and frequent infection play an important part.

The ill health and the relation of rheumatism to heart disease make the subject of great economic importance. In young patients, the heart may be involved in as high as from 70 to 90 per cent. Immunity does not develop, and relapses may occur after several years. In children, rheumatism may be almost symptomless except for the common involvement of the heart. Lyon discusses the treatment especially with salicylates and regards them as only palliative, making necessary better methods of treatment. Continued supervision for years, prevention of recurrent disease and a prolonged period of convalescence with special training in accordance with physical capacity will help rheumatic persons to acquire a better degree of health and economic usefulness.

Gilchrist proceeds with the discussion, dwelling on the most important factor of cardiac damage in which the beginnings are most often in the ages between 5 and 15 years. The ordinary hospital care does not give the best results for

the individual, the hospital or the community. The rheumatic suspects should be discovered in the schools, kept under supervision, and the homes, care, rest, convalescence, research and education of the patients supervised. England now has ten hospital-schools for patients recovering from rheumatism. Such a school is the one at Birmingham, in which permanent benefit apparently results after a residence of not less than six months. A large proportion of the children there leave either without having the heart involved or after recovering from cardiac disease. Gilchrist recounts the other places in England and Scotland where notable work is being done. Edinburgh has the highest rate for rheumatic heart disease in Scotland, the incidence amounting to 13 in each 1,000 children. Gilchrist believes that the physicians and the public health officials and medical officials of the schools should unite in an effort to check or discover the disease.

NEFF, Kansas City.

ACUTE ARTICULAR RHEUMATISM IN CHILDREN. GRENET and DELALANDE, Arch. de méd. d. enf. **31**:453, 1928.

Thirty-two cases of rheumatic fever in children seen in the course of a year are reported, with exhaustive comment on the inconstant clinical picture, the complications and particularly the medical treatment. These children varied in age from 5 to 15 years, the largest number of cases occurring at the age of 11. The onset in most instances was marked by distinct manifestations in the joints, but in nine cases distinct angina was present; it appeared coincidentally with the arthritis, yet was accompanied by so little pain and discomfort that it could readily have been overlooked. Particular stress is made by the writers on this point. Further symptoms commonly noted with the onset of rheumatism were diarrhea (two cases), constipation (frequently) and vomiting (one case). With reference to articular involvement, most of these children exhibited the classic symptoms usually associated with the disease. There were some cases, however, four in all, which showed a complete absence of attacks of rheumatism in the joints, the brunt of the invasion apparently being carried by the heart. One case was ushered in with cardiac collapse; later, pericarditis developed. Another merely showed signs of a grave infection followed by endocarditis, without arthropathies of any sort. Seven months later, this child developed chorea which responded readily to arsenicals. A third case of masked rheumatism in a boy of 10 years was characterized by profound prostration, anemia, high temperature and endocarditis. This patient responded promptly to massive doses of salicylates. The remaining subject, a boy of 7, suffered from persistent fever, emaciation and weakness and was treated for tuberculosis for a month before rheumatism was suspected. By this time the mitral endocardium was seriously involved. Salicylates restored this child to health with the exception of regurgitation, which persisted.

Among the thirty-two cases studied, twenty-five showed development of definite lesions in the heart, either frank endocarditis, pericarditis or endopericarditis; this agrees with Weill's observations at Lyon, but the incidence is higher than that noted in the series reported by Besnier who found only 50 per cent showing cardiac damage. With respect to treatment, Grenet and Delalande recommend and used much larger doses of the salicylates than are usually prescribed by American physicians. They do not hesitate to employ from 6 to 8 Gm. for a child under 10 and give as high as 10 Gm. to a child over that age. When the gastro-intestinal tract shows marked intolerance, the intravenous method is employed or when this is impracticable, the drug is given by rectum. In resistant cases in which the salicylates have been exhibited freely for several days without marked relief, these clinicians have employed with success intravenous injections of colloidal gold (collobiase Dausse). For thirteen years, Grenet has found it a valuable agent in intractable rheumatism and believes that it should be used early enough to avert cardiac injury.

AMESSE, Denver.

WHOOPING COUGH IN CHILDHOOD. W. MIKULOWSKI, Rev. franç. de pediat. **4**: 185, 1928.

The author believes that whooping cough has been considered entirely too casually by the medical profession. Instead of regarding it as a passing contagious disease, he believes that the infection often remains latent in the lungs over a period of years. The lung so infected, under the influence of a mixed grippal infection or, particularly, measles, is the frequent root of serious pulmonary complications, such as pleurisy, bronchiectasis or gangrene. The condition may be confused with tuberculosis. The paper is suggestive, although one is not convinced that all the cases cited actually were an exacerbation of an old whooping cough. The bacteriologic evidence is lacking, as is also evidence which might have been gathered from differential blood counts.

LESLIE, Evanston.

DIPHTHERIA. MARTINEZ VARGUS, La med. de los niños **29**:1 (Jan.) 1928.

A review of the patients with diphtheria who entered the hospital during the last six months of 1927 showed a mortality rate as follows: Total cases, eighty-six; faucial diphtheria, three cases, in all of which recovery occurred; laryngeal diphtheria, fifty cases, with a mortality of 12 per cent, and diphtheria with bronchopneumonia, thirty-three cases, with a mortality of 45 per cent.

Faucial diphtheria was rare in early infancy, and the laryngeal type prevailed. Either intubation or tracheotomy was done on every patient (eighty-three intubations and three tracheotomies). The dose of antitoxin varied from 20,000 to 50,000 units, the first dose being given on admission and the second twelve hours later. Further doses were given every twenty-four hours.

The disease is prevalent in Spain, and the mortality is unusually high. Stations are being established for the gratuitous administration of toxin-antitoxin in Barcelona.

DWYER, Kansas City.

THE TREATMENT FOR SCARLET FEVER. MARTIN GONZÁLEZ-ALVAREZ, Pediatría españ. **17**:139, 1928.

The author discusses the treatment for scarlet fever as generally practiced today in Spain.

For the endemic form, rigorous isolation of the patient and hygienic measures for all infectious, contagious processes are sufficient to prevent the spread of the disease. The method of treatment suggested by Milne is recommended, if carried out by trained personnel.

For the epidemic form of scarlet fever, active vaccination with scarlet fever toxin or passive vaccination with serum is used as a preventive measure, according to the urgency of the case. These measures are always preceded by a Dick test.

A dietetic-hygienic regimen has generally been found sufficient in the mild forms. In severe and malignant forms, serum therapy (in most cases in the form of antitoxin) is used from the beginning of the disease. On account of the usually benign nature of this disease in Spain, prophylactic vaccination is not widely practiced nor is the use of serum therapy general.

SCHLUTZ, Minneapolis.

NUTRITION AND SCARLET FEVER. WILHELM SCHLIEPS, Jahrb. f. Kinderh. **120**:127 (June) 1928.

In an extensive article on the relationship of the state of nutrition to the incidence of scarlet fever, Schlieps notes that it has been known for a long time that there is no general susceptibility to scarlet fever. Approximately one third of all children exposed contract scarlet fever. The writer notes that in recent times more emphasis has been placed on the bacterial agent of scarlet fever than on the person contracting the disease.

Czerny was the first to state definitely that there was a relationship between the state of nutrition and immunity to scarlet fever. In May, 1911, he remarked

in his clinical lectures that improperly nourished children with exudative diathesis were more susceptible to scarlatina.

From the writer's personal experience in South Russia before and during the World War, he noted that when food was readily obtainable and the children were excessively well fed with milk and eggs, there were more cases of scarlatina and a more serious type than when there was a comparative scarcity of food and the diet was simple. Overnourished children offer a poorer prognosis than normally nourished children.

As a predisposing cause to scarlatinal infection, the author considers previous and repeated nasopharyngeal infections and a pathologic condition of the mucous membranes. Children of the exudative diathesis group fulfil these conditions and as a rule suffer from a severer type of scarlatina with complications. Children not of this diathesis group but improperly nourished usually have a light form of scarlatina without complications. Rationally nourished children who are not of the exudative diathesis group do not contract scarlet fever.

The best form of scarlatinal prophylaxis is nutritional prophylaxis.

THE HEINE-MEDIN EPIDEMIC OF 1926 IN HUNGARY. J. VON BOKAY and JENO VAS, Jahrb. f. Kinderh. **119**:253 (April) 1928.

Bokay and Vas describe an epidemic of poliomyelitis and present a curve of the incidence of the cases and maps of the localities involved. Among the 252 patients there were 136 boys (53.6 per cent) and 116 girls (46.4 per cent). The age distribution was as follows: under 1 year, 22.3 per cent; between 1 and 3 years, 56.3 per cent; from 2 to 7 years, 21.2 per cent; from 7 to 14 years, 1.6 per cent; older than 14 years, 0.8 per cent. Thus, 78 per cent of the cases occurred during the first three years of life. Two adults were affected.

The curve of the epidemic shows the highest incidence of cases in the months of July, August and September.

As to the types of cases, the most frequent involvement was of the lower extremities (22.5 per cent). There were five cases of Landry's paralysis, all with a fatal ending.

Healing with complete restitution of function occurred in 7.9 per cent of the cases. (In 1911, this figure was 4 per cent.) There were eleven deaths (4.3 per cent).

The maps show that the condition is an infectious one. The author found the focus of the epidemic on the Donau River and predicted a spread along the various lines of travel from this center.

ARTHUR ABT, Chicago.

EPINEPHRINE THERAPY. T. SCHÖNFELDER, Acta Paediat. **7**:95 (April) 1928.

Since acute infections are often followed by asthenic states which may be ascribed to failure of the function of suprarenal glands, Schöfelder attempted to determine this point by giving to patients convalescing from diphtheria 20 drops of epinephrine solution either subcutaneously or by mouth, later determining the effect on the blood sugar. Following mild diphtheria, there was a minimal effect on the blood sugar curve, but following a few cases of severe diphtheria, a pronounced elevation of blood sugar level appeared and persisted for three or four weeks, coinciding with a lowering of blood pressure. No conclusions were drawn.

THE ETIOLOGY OF SCARLET FEVER. A. LICHTENSTEIN, Acta Paediat. **7**:106 (April) 1928.

Lichtenstein reports the recent experience with scarlet fever in the Stockholm Epidemic Hospital. Hemolytic streptococci were recovered from the throats of 90 per cent of 650 patients with scarlet fever; in 65 per cent they persisted up to the time of discharge from the hospital, six or eight weeks after the onset. Dick tests made on 2,600 unselected persons showed a curve of age incidence of positive tests conforming closely to the age incidence curve of 1,783 patients with scarlet

fever. When Dick tests were made once a week in patients known to have scarlet fever, it was found that more than 60 per cent reacted positively during the first week of the disease; that the curve of positive reactions plotted against time fell gradually until, in the eighth week, there were only 9 per cent of positive reactors. When the cases showing relapse were separately plotted, positive reactions were obtained more frequently and persisted longer. In some patients the reaction shifted from positive to negative and back again in an entirely irregular fashion, and this feature was especially well brought out by making tests every day for five or six weeks. Single tests, therefore, have much less value than repeated tests. The fact that a higher proportion of positive reactions was obtained with a toxin of local manufacture than from an imported sample was interpreted to indicate a regional strain specificity. Both convalescent serum and Dick antitoxin were effective in the author's hands in changing a positive skin test to negative, and in the treatment for severe forms of the disease. Immunization by injections of Dick toxin also effectually changed positive reactions to negative; but during the course of such prophylaxis the positive reaction may for a time appear more quickly, just as a tuberculin reaction may appear more quickly during treatment with tuberculin. The number of patients showing complications was too small to permit conclusions to be drawn regarding the effect of serum in this respect.

SCARLET FEVER: IV. IMMUNITY OF THE NEW-BORN TO SCARLET FEVER. A. LICHTENSTEIN, Acta Paediat. **7**:121 (April) 1928.

One hundred mothers and their new-born infants were studied by the Dick test. The serums of a number of women giving positive and negative reactions to the Dick test were tested for antitoxin content by the extinction test, and samples of blood from the umbilical cord from the infants of the same women were similarly tested for antitoxin. Control tests for the presence of antitoxin were carried out by neutralization of toxin. Finally, Lichtenstein made both extinction test and neutralization test with milk, and in one case with colostrum, from mothers giving positive and negative Dick reactions. He concluded that mothers with negative Dick reactions have children with negative Dick reactions; that mothers with positive Dick reactions usually have children with negative Dick reactions, but that in a certain proportion of cases the children react positively also; that serum from mothers with negative Dick reactions shows evidence of specific antitoxin, and that cord blood from the infants of these mothers likewise contains antitoxin; that the cord blood of infants with negative Dick reactions with mothers of positive Dick reactions does not contain antitoxin; that there is no evidence that scarlatina antibodies reach the infant through the mother's milk, but, on the other hand, there is good evidence that they may be transferred through the placenta. The insusceptibility of certain infants to scarlet fever, in the absence of demonstrable antibodies in their blood, causes the author to postulate that special conditions obtain at this age, and that they must be interpreted as phenomena of allergy rather than immunity.

McINTOSH, Baltimore.

DIPHTHERITIC CONJUNCTIVITIS. HOLGER EHLERS, Ugesk. f. Laeger. **90**:823 (Aug. 23) 1928.

The occurrence of diphtheritic conjunctivitis in four children and two adults is described. In two of the patients, it involved both eyes; in four it was unilateral. The early use of antitoxin may prevent spread to the opposite eye.

The use of antitoxin locally was suggested by the author but was not tried. Frequent irrigation of the eyes with physiologic sodium chloride solution and the injection of serum were the therapeutic measures employed.

SCHLUTZ, Minneapolis.

LIGHT FORMS OF SCARLET FEVER. Z. L. KOFMAN, Pediatriya **11**:137, 1927.

The main object of this work was to analyze all light cases of scarlet fever in order to find out what is the percentage of them observed in the clinics, how often they show complications, and the death rate. The material is the result of six years of observation and represents 680 cases, from which 106 light cases were studied.

The conclusions are as follows:

1. The light form of scarlet fever is characterized by minimum local changes in the throat (angina catarrhalis) which do not reach necrosis; light general manifestations in the nervous system and light phenomena of intoxication.

2. Among complications which the light cases of scarlet fever show are: (1) myocarditis with its accompanying changes and symptoms (75 per cent); (2) acute lymphadenitis with pus (40.5 per cent); (3) otitis (23.7 per cent, in 14 per cent of which pus formed); (4) nephritis (14.5 per cent). The prognosis depends on the complications in the kidneys—nephritis.

3. The death rate in light cases of scarlet fever is 1.9 per cent, and death occurs mostly in cases complicated with nephritis.

4. The constitution of these children was farily good, at least as far as can be gathered from measurements. Their infancy had been normal.

5. A large percentage of the children who develop nephritis have an alcoholic or tuberculous heredity on which the prognosis depends in such cases.

ASCHNER'S PHENOMENON IN SCARLET FEVER. S. K. MIROSHKINA, Pediatriya **11**:147, 1927.

The author's problem was to observe Aschner's symptom during the course of scarlet fever.

He examined fifty-two children from 2 to 14 years of age. Children below 2 years could not be examined because they could not be kept sufficiently quiet. The reflex was observed every morning at the same hour, from the time of entrance of the child into the hospital until his departure. The technic of the examination was that of the French school.

During the first five days of the disease, Aschner's symptom is negative or normal. The author made sixty-five observations during this period, and in 24.3 per cent of the cases Aschner's symptom was negative, in 39 per cent it was normal, in 12.5 per cent positive and in 15.7 per cent very positive. From the fifth to the twenty-first days, Aschner's symptom was positive and very positive. In fifty-one observations during this period, Aschner's symptom was negative in 3.9 per cent of the cases, normal in 33.3 per cent, positive in 27.5 per cent and very positive in 35.3 per cent. From the twenty-first day on, Aschner's symptom became normal in 60 per cent of cases. In sixy-one observations made during this period, the positive and very positive reflexes fell from 62.8 per cent of the previous period to 37.3 per cent. The normal reaction increased from 33.3 to 59 per cent. The negative reaction was 3.3 per cent.

Thus Aschner's symptom is very positive from the fifth to the twenty-first day. During the epidemic of scarlet fever, a few of the children caught measles and rubeola during the later period of scarlet fever, and they showed very positive Aschner's reaction in the period when the Koplik spots appeared.

SEVERAC, Philadelphia.

A COMPARATIVE STUDY OF TUBERCULIN AND VACCINE THERAPIES FOR PERTUSSIS. MISAO MATSUDA, J. Pediat. (Tokyo), Aug. 20, 1928, No. 339, p. 1312.

In 1925, Stuhl first published what may be called a successful therapy for pertussis by means of old tuberculin. Matsuda here reports his experience in the

results obtained by applying tuberculin in forty cases and pertussis vaccine in thirty-two cases of whooping cough in the pediatric service of the Hokkaido Imperial University. He finds that when tuberculin was used, there was improvement of symptoms in 47.5 per cent of the cases, while vaccine produced improvement in 59.4 per cent. In infants under 1 year of age, both cough and vomiting were ameliorated in 42.8 per cent with vaccine and in 28.6 per cent with tuberculin, but in infants aged from 1 to 2 years, there was improvement in 71.4 per cent with tuberculin and in 57 per cent with vaccine. Thus, it may be concluded that while tuberculin is not a specific for whooping cough, it may be employed as one of the means of treating it.

KATO, Los Angeles.

Chronic Infections

SEX DIFFERENCES IN THE PATHOLOGIC PICTURE OF SYPHILIS. ALDRED SCOTT WARTHIN, Am. J. Syph. **12**:301 (July) 1928.

The incidence of syphilis is probably about equal in the two sexes. The primary lesion is much less severe and is less frequently noted in the female than in the male. The cervix and nipple, however, are an exception to this rule, a cervical chancre being large and indurated and on inspection closely resembling cancer. The breast also is frequently removed because of a diagnosis of cancer. A chancre of the clitoris or urethra is also large.

The skin rash of the secondary stage is much less marked, and may be absent, especially during the child-bearing period. The other symptoms, toxemia, ostealgia, rheumatic manifestations and anemia, are more marked than in the male. Many women in this stage give a negative Wassermann reaction. Renal and hepatic involvement are more common in the female. Leukoderma coli and vitiligo are rarely seen in the male.

In the majority of syphilitic women the disease becomes latent during the child-bearing period; the Wassermann reaction may be constantly negative. These women may repeatedly give birth to syphilitic children. At the time of the menopause, the Wassermann reaction may become positive and the symptoms reappear. The central nervous and cardiovascular system is much less involved than in the male. The liver, pancreas, suprarenals, rectum, subcutaneous tissue and periosteum are more commonly involved in females. Many go through life without a single suggestion of syphilis.

Syphilitic lesions are found in the heart and aorta in practically 100 per cent of syphilitic males. They are rarely found in females. The liver is much more frequently involved in the female than in the male, the ratio being about 25 : 1. The chief form is that of hepar lobatum. This condition is rarely diagnosed during life. The involvement of the spleen is parallel to a degree with the involvement of the liver and is therefore more pronounced in the female.

Syphilis of the stomach is not common in the male but is much rarer in the female, the ratio being about 9 : 1. Syphilis of the gastro-intestinal tract in the female is of importance only in the rectum, being found about twenty-five times as frequently as in males.

The suprarenals are involved much more frequently in females than in males, this being the location in which spirochetes are most frequently found in latent syphilis of the female.

There is no evidence that the ovary is ever involved; this is in marked contrast to the testis. If one examines the heart, aorta and testes of a man, one can tell whether or not he has syphilis, but examination of the heart, aorta and ovaries of a woman reveals little if any evidence as to this point. The tubes have not been found to contain gumma in the author's experience.

The central nervous system of the female seems to be much more immune to syphilis than that of the male, the ratio being 3 or 4 : 1.

MODERN METHODS IN THE TREATMENT OF SYPHILIS. BASED ON A SURVEY OF THE LITERATURE OF THE PAST FIVE YEARS AND THE ADMINISTRATION OF MORE THAN THIRTY THOUSAND TREATMENTS. ALFRED E. JONES, Am. J. Syph. **12**:374 (July) 1928.

The author concludes from the literature and from his own experience that silver arsphenamine is a most effective preparation in the treatment for syphilis, its disadvantage being the degree of irritation produced when part of the solution escapes from the vein.

Sulpharsphenamine is of particular value in the treatment for congenital syphilis, since it is nonirritating when given intramuscularly and is efficacious.

When administered intramuscularly, bismuth compounds have proved to be a useful addition to the usual method of treatment, their spirocheticidal index lying between that of arsphenamine and mercury.

Every patient with syphilis should be given at least one course of mercury in conjunction with the other drugs. The best means of administration is by the inunction method.

Flumerin, given intravenously, has also been proved an efficacious method of administering mercury.

McBRIDE, Sioux City, Iowa.

THE DIAGNOSIS AND PROGNOSIS OF JUVENILE TUBERCULOSIS. HENRY D. CHADWICK, Boston M. & S. J. **197**:1399 (Jan. 26) 1927.

This paper is based on the examination of 50,000 school children between the ages of 5 and 15, an investigation carried on during the last three years by the Massachusetts Department of Public Health as a part of the ten year program for the prevention of tuberculosis and on the author's experience as superintendent of the Westfield State Sanatorium, an institution having 300 beds devoted to the care of tuberculous children.

Hilum tuberculosis is the term used to designate the juvenile type of tuberculosis. Following a first infection, a primary nodule develops in some part of the parenchyma of the lung, and the tracheobronchial lymph nodes draining that area become infected and diseased.

Diagnosis was made by considering the following factors:

History.—Evidence of contact with an open case of pulmonary tuberculosis is important, as four times as many cases of pulmonary tuberculosis were found among the contact children as were found among the children without a history of exposure.

Symptoms.—Undue fatigue, lassitude, anorexia and nervous irritability are the most common symptoms. Cough and fever, so often present in pulmonary tuberculosis, are rarely found in the juvenile type.

Tuberculin Test.—A positive Pirquet or intracutaneous tuberculin test is essential to make certain of infection. In children aged from 5 to 15 years, a positive reaction may not indicate active disease, but it probably does mean that the child is harboring living tubercle bacilli. The question of activity must be determined by symptoms and the general physical condition. The percentage of reactors gradually increases from 20 at 5 years to 35 at 15. The intracutaneous test is a little more accurate but is not practical to use in school clinics.

X-Ray Examination.—A roentgenogram is the most valuable aid in the study of these children. Without it, an absolute diagnosis of hilum tuberculosis cannot be made, nor is a physician justified in eliminating tuberculosis as a possible cause of ill health in a child unless the roentgenogram is found to be negative.

Doctors Opie and McPhedran, of the Phipps Institute, in their studies of the lungs of children who had died of diseases other than tuberculosis, have demonstrated that enlarged tracheobronchial glands appear only as opaque shadows in a roentgenogram when they contain a deposit of calcium; also that calcium is deposited in glands or nodules only when they are tuberculous.

Latent hilum tuberculosis is a term used to describe the cases of juvenile tuberculosis often found in children in whom there are no physical signs or symptoms of disease. The roentgenogram, however, may show calcified masses at the hilum or one or more nodules in the lung. The tuberculin test is positive, from which one can conclude that living tubercle bacilli are present. In such cases, an unstable immunity exists. A lowered resistance, due to an intercurrent disease, a reinfection from the child's own focus or from outside sources, may quickly convert a latent case into an active one.

Incidence of Infection.—Statistics from the State Clinic show that 29.7 per cent of nearly 25,000 children between the ages of 5 and 15 reacted to the Pirquet tuberculin test. As this group was made up of 17 per cent contacts and many underweight children (about 37 per cent), this percentage is considerably higher than the average would be if all the children were given the test with no attempt at selection. The percentage of reactors among the contact children was nearly twice as high as among the group of noncontact children. One community that had been colonized extensively by tuberculous families had a high percentage of reactors.

The rural group showed 28.5 per cent reactors as compared with 29.9 per cent for the urban children. All the school children in three small towns were given the tuberculin test, and the reactors averaged 16 per cent. As the small towns throughout the state averaged 2.4 per cent less reactors than the urban communities, it would seem equitable to add this difference to the rate found in the towns and consider from 18 to 20 per cent as the state-wide average.

It is interesting to compare the results obtained by the examiners from the State Clinic in 1926, in Framingham, with those found by Dr. P. C. Bartlett in the work he did for the Framingham Demonstration in 1917. Dr. Bartlett gave the tuberculin test to 460 children from 1 to 7 years of age and found 33 per cent of them infected. At the State Clinic 520 children from 3 to 15 years of age were examined, and 25.5 per cent reacted to the tuberculin test. When these children were divided into age groups, it was found that those in the Demonstration group, aged from 5 to 7 years, showed 52 per cent reactors and that those in the State Clinic group of corresponding age showed only 14.2 per cent, a decrease of 38 per cent.

The Incidence of Tuberculous Disease.—In the State Clinics, in 12.5 per cent of the reactors the condition was diagnosed as hilum tuberculosis; in an additional 35 per cent the reactors were classified as suspects; 47.5 per cent of the reactors, therefore, appeared to be in need of special care or treatment. This would be equivalent to between 9 and 10 per cent of the whole school population below the high school grade. This estimate does not seem to be excessive when one studies the death rate from tuberculosis.

Last year, 6.5 per cent of all deaths in Massachusetts were from some form of tuberculosis. Eighteen per cent of these were in persons under 20 years of age. But fifty school children of 25,000 could be classified as having the adult type of pulmonary tuberculosis.

Prognosis.—Experience shows that the children with hilum tuberculosis, who are treated in the sanatorium long enough to reach average weight, develop good musculature and live the normal child's daily life without undue fatigue and remain well after discharge, provided the conditions at home are reasonably good.

Corroborative evidence that many school children have hilum tuberculosis is obtained by the examination of older students. Roentgenograms of 3,800 students in colleges, normal schools and high schools were taken. Only 900 of this group were in the high schools. The investigators found 6 students with the pulmonary type of tuberculosis, and 231 had the latent hilum type of the disease. This is 6 per cent of the whole number. The lesions had been in existence some years, as the students had well calcified pulmonary nodules or tracheobronchial glands.

The author concludes that about 20 per cent of the school children in Massachusetts are infected with tubercle bacilli, as shown by the Pirquet tuberculin

test. Approximately one half of these have signs or symptoms or roentgenographic evidence of the juvenile type of tuberculosis.

It is probable that many of the deaths from tuberculosis that occur during adolescence and early adult life are the result of massive infection in childhood that was unrecognized and untreated. Chadwick also finds that in the early pulmonary form in children, if the condition is found and treated before tubercle bacilli are present in the sputum, the prognosis is good. If, however, these secondary lesions go on to the ulcerative stage and bacilli are set free, then the patient, if under 16 years of age, will almost invariable die of pulmonary tuberculosis, regardless of what treatment is given.

GENGENBACH, Denver.

TUBERCULOUS INFECTION IN INDUSTRIAL SCHOOL CHILDREN. A. FERGUS HEWAT, Edinburgh M. J. **35**:451 (Aug.) 1928.

Hewat emphasizes the importance of using the school rather than the hospital for starting research into tuberculous infection, by discovering infected children and following the investigation into the home. He studied a series of sixty school boys from industrial homes for the poor, noting the physical examination, vital capacity and the roentgenographic manifestations. The degree of infection was determined by the correlation of the result of the Pirquet test with the cervical glandular enlargement.

Hewat believes with Sir Robert Philip that a search of all the superficial glandular areas of the body gives significant results in that numerous supraclavicular lymph nodal enlargements are as important as large lymphatic glands in pointing to tuberculous disease. When the presence of such glandular enlargement is studied with reference to tuberculin tests and postmortem examinations, it is seen that the lymphatic system has been greatly involved as a primary tuberculous infection.

In Hewat's investigation, the Pirquet method of skin testing was used. Both human and bovine tuberculin were employed in each child, the bovine never causing a positive reaction unless the human did also. The reaction with human tuberculin was more intense than with the bovine. Only in patients 10 years of age were the number of positive reactions more common than in the other groups from 5 to 14 years of age. It was found that palpable cervical glands, often numerous and of moderate size, are nearly twice as common in infected as in uninfected children.

NEFF, Kansas City.

THE RÔLE OF THE SKIN IN TUBERCULOSIS. P. WORRINGER, Rev. franç. de pediat. **4**:170, 1928.

New experimental work is not offered in this article, but the author presents his argument from well established observations. He concludes that two modes of immunization against tuberculosis have their origin in the skin; the one, nonspecific (dermophylaxis), depending on irradiation and general stimulation of the skin, the other, specific (dermoantergy), developing following a tuberculous skin infection or a cutaneous vaccination. He distinguishes between these two factors and allergy, which he does not think is necessarily related to immunity.

LESLIE, Evanston.

MANAGEMENT AND FATE OF SYPHILITIC CHILDREN. KURT FÜRST, Jahrb. f. Kinderh. **119**:355 (April) 1928.

Due to the conflicting views and methods as to results in the treatment of syphilitic children, Fürst has studied the material of the Frankfurt Dermatological Clinic, comprising 422 cases of congenital syphilis and 21 children with acquired syphilis. To this was added reports of 292 cases from the Children's Clinic, making a total of 735 cases.

The mortality in 681 cases of congenital syphilis was 50 per cent. The largest cause of mortality was pneumonia.

In autopsies performed on 80 children, there were observed the following syphilitic changes in the internal organs; splenomegaly, hepatitis, miliary gumma of the liver, gumma of the lungs, pneumonia alba, osteochondritis syphilitica, gumma of the heart, gummatous cystitis and nephritis.

Approximately half of the congenital syphilitic patients had syphilitic eruptions similar to secondary manifestations in the adult. Of these, 50 per cent died, showing a high mortality in children with syphilitic exanthems.

Serologically, 85 per cent showed a positive Wassermann reaction of the blood.

The treatment consisted of mercury, bismuth compounds and neoarsphenamine, a rigid plan not being followed. Mercury was also given in the form of rubs, baths, etc.

Neoarsphenamine was given in gradually increasing doses of from 0.045 to 0.075 Gm. and from 0.10 to 0.15 Gm. The dosage was discontinued for from four to six weeks and then repeated according to indications.

Bismuth compounds have been used much in recent years, since they are well borne by children. They are injected intramuscularly in doses of 0.2, 0.5 and 1 Gm., according to the age.

Of the total number, it was possible to follow up thirty-nine cases. Nine cases did not show physical or mental changes due to syphilis. Sixteen cases still showed physical signs of syphilis. There were nine instances of psychic defects. Twenty-five were normal mentally.

There were twenty-one instances of acquired syphilis in the series comprising thirteen girls and eight boys. In these the results are more favorable than in congenital syphilis and not any worse than in the adult acquired form.

It is thought that better results were obtained with combined arsphenamine and mercury or arsphenamine and bismuth compounds than with mercury alone.

No harmful effect on the nervous system was noted with arsphenamine.

THE INFLUENCE OF EXTERNAL FACTORS ON THE SUCCESSFUL TREATMENT OF CONGENITAL SYPHILIS. PAUL VON KISS, Jahrb. f. Kinderh. **120**:88 (May) 1928.

Paul von Kiss attempts to answer the question as to the most satisfactory age at which permanent and curative results are obtained in the treatment for congenital syphilis, as shown by the Wassermann reaction. He has studied the records of 133 patients who were treated uniformly. During the first year, three courses of combined bismuth compound neoarsphenamine cures were administered. During the rest periods, the proto-iodide of mercury, potassium iodide or mercury rubs were given. During the second year the foregoing dosage was administered at six month intervals.

The results were studied statistically in various tables according to age groups and Wassermann reactions. In the first table it is shown that the larger percentage of negative Wassermann reactions (59.42 per cent) occurred in the group treated in the first three months. The second table shows that the largest percentage of positive Wassermann reactions occurred in those first treated after the age of 7 years (34.37 per cent). Another table which shows those whose Wassermann reaction was negative after two years without treatment showed 56 per cent of those who had received treatment in the first three months and none who had received treatment after the age of 7 years. Of those treated during the first year, 80 per cent showed a negative Wassermann reaction, and after the first year, only 20 per cent. Of twenty-five cases in which cure was effected, only 4 per cent occurred in the patients treated after the third year.

Von Kiss concludes that the best practical results are obtained when antisyphilitic treatment is administered during the first three months of life; the next best results are obtained by vigorous treatment during the first year.

THE RELATIONSHIP OF END-RESULTS IN THE MANAGEMENT OF CONGENITAL SYPHILIS TO THE CONSTITUTIONAL FACTORS. PAUL VON KISS and FRANZ SKROPP, Jahrb. f. Kinderh. **120**:96 (May) 1928.

In this investigation of 114 patients with congenital syphilis, von Kiss and Skropp attempted to study the relationship between the results of specific therapy to the various blood groupings of the persons. Verzar's blood grouping is used throughout; O, A, B, AB when O is not agglutinated by any serum, A is agglutinated by B, and B by A, and AB is agglutinated by all three. This nomenclature corresponds to the Jansky I, II, III, IV, and the Moss IV, II, III, I.

The work of Stranzynsky is mentioned in which it is shown that the Wassermann reaction of those in group O is more readily and favorably influenced by treatment and that of group AB the most resistant to treatment.

In the author's group a difference was not noted among the various blood groupings with respect to rapidity of disappearance of clinical symptoms under treatment.

The following interesting table is presented:

Group	Number of Patients	Became Negative Under Treatment	Remained Positive	Percentage Negative; Wassermann	Percentage Positive; Wassermann
O.....	40	27	13	67.5	32.50
A.....	52	32	20	61.53	38.45
B.....	13	7	6	53.84	46.16
AB.....	9	4	5	44.4	56.56

Those in group O were more susceptible to treatment, as determined by the negative Wassermann reaction, than those in group AB.

Further, it was found that of the patients giving negative Wassermann reactions those in group AB showed the most frequent tendency to have a positive reaction later and those in group O, the least tendency to have a relapse. The largest percentage of positive Wassermann reactions after two years' treatment was in group AB (group I, Moss). Group AB showed most unfavorable fluctuations and tendency to relapse.

TWINS WITH CONGENITAL TUBERCULOSIS. K. CHOREMIS, Jahrb. f. Kinderh. **120**:319 (July) 1928.

Choremis ascribes to congenital tuberculosis a more conspicuous place than it has received in the past. According to Scheer, 5 per cent of all tuberculous infants have congenital tuberculosis.

The author reports two infants (twins) who were admitted to the institution from a foundling home. The infants weighed 3,250 and 3,080 Gm., respectively, at 3 weeks of age and seemed sufficiently well developed for their age. A routine tuberculin test showed a marked positive reaction in both infants. A detailed family history was not available.

One infant (weighing 3,250 Gm.) seemed well nourished and was started on a half-milk dilution. Several days after admission, the infant began to show a febrile reaction. The physical examination showed impaired resonance at the base of the right lung and fine crackling râles on auscultation. Gradually, the general nutrition became impaired; the child developed diarrhea, lost weight and died at the age of 5 weeks. The autopsy showed a general tuberculosis with dense infiltration of the hilum and base of the right lung, caseation of the hilum glands and involvement of the spleen and mesenteric glands.

The other infant (weighing 3,080 Gm.) had no febrile reaction. The state of nutrition was good. Three days after admission, the infant began to suffer from vomiting and diarrhea. The weight gradually declined, and the infant died

under the clinical picture of a nutritional disturbance. Autopsy showed caseation of the tracheobronchial glands, miliary tuberculosis of the lungs, tubercles of the spleen and enlarged mesenteric glands.

The author considers this to be a genuine congenital tuberculosis, the result of intra-uterine infection, belonging to Moll's early form of congenital tuberculosis. Further, the author thinks that this was the result of a purely hematogenous infection with tendency to localize in the pulmonary tissues.

ARTHUR ABT, Chicago.

TUBERCULOSIS IN THE FIRST THREE YEARS OF LIFE. V. POULSEN, Acta paediat. **7**:158 (April) 1928.

Ninety-nine tuberculous patients under 3 years of age were studied, exclusive of those with tuberculous meningitis. Proof of the diagnosis depended on tuberculin tests or on the results of autopsy. Eighty-six patients of the group gave either a positive Pirquet or a positive Moro test; in five of the remaining patients, the Mantoux test was positive. In three patients all reactions were negative, but tuberculous lesions were found after death. The mortality figures confirmed the general opinion that the prognosis is more grave the younger the patient. Of the entire group, thirty-four had only glandular tuberculosis, and none of these died; sixty-five had pulmonary or intestinal involvement, and forty of these died. The therapeutic measures used were sunlight, fresh air, a high caloric diet, cod liver oil and ultraviolet light from the mercury vapor quartz lamp. Five patients were treated with sodium aurothiosulphate, all of them showing pulmonary involvement; four of them were alive at the time the paper was written, two of them 2 years of age, the others 3. The injections were given intramuscularly and were not attended with serious disturbances although large doses occasionally gave rise to transitory fever or albuminuria or loss of weight. The author is not willing to say whether sodium aurothiosulphate helped these patients, but he feels that it did not harm them in the moderate dosage used.

FOLLOW-UP STUDY OF PATIENTS WITH POSITIVE TUBERCULIN TEST. H. SÖDERSTRÖM, Acta paediat. **7**:167 (April) 1928.

Since 1909, Söderström has encountered 235 patients under 2 years of age showing a positive tuberculin test, and he was able to obtain information on 225 of these. Of this number, 134 died of tuberculosis, 25 of other diseases and 66 were still alive. The mortality of the entire group of children showing a positive test during their first year of life was 63.7 per cent; of the group showing a positive test for the first time during their second year, it was 50.6 per cent. Of the 134 that died, all but 5 died during their first or second year. The mortality of those in whom a diagnosis of the pulmonary form was made reached 89.8 per cent. Of the 66 surviving patients from the entire group, 63 were personally followed. Their average age was 10½ years, with a range of from 5 to 17 years. Seventy per cent were in good health; active tuberculosis was present in only 10 per cent, while another 10 per cent were healthy but delicate.

MCINTOSH, Baltimore.

THE USE OF B.C.G. VACCINE IN COMBATING TUBERCULOSIS IN INFANTS. K. A. JENSEN and E. HUSTED, Ugesk. f. Laeger. **90**:651, 1928.

A critical review is presented of the results obtained with Calmette's B.C.G. strain of tubercle bacilli. Up to the present time 90,000 infants and children have been vaccinated, and from the abbreviated reports of many workers, it appears that immunization is realized to some degree.

With the exception of the views held by Petroff, there is general agreement that the vaccine does not produce the disease. He, however, demonstrated that two strains were present in a B.C.G. culture and that one of these was pathogenic for laboratory animals.

POSITIVE TUBERCULIN REACTIONS. ERIK HUSTED, Ugesk. f. Laeger. **90**:727, 1928.

In 604 patients of all ages, studies were made of positive tuberculin reactions. About 10 per cent of the children under 5 years of age showed a positive reaction. The increase of positive reactions was rapid up to 40 years of age; then there was a steady decrease as senility approached. Several explanations are offered for this diminution of positive reactions in later years. The author thinks it possible that the reaction becomes less and less positive as the original infection burns out.

SCHLUTZ, Minneapolis.

APPEARANCE OF RETICULATED SUBSTANCE IN ERYTHROCYTES IN CONGENITAL SYPHILIS. TETSURO SHINDO, J. Pediat. (Tokyo), Aug. 20, 1928, no. 339, p. 1304.

The author studied the appearance of reticulated substances in nineteen patients with congenital syphilis in Osaka Medical College Hospital. The reticulated substances are classified according to their shape as: type I, which is called substantia reticulofilamentosa, the reticulated substances being in chain formation by means of filaments, and type II, known as substantia metachromaticogranularis or substantia filamentogranularis, the reticulated substance being seen in granules and more or less evenly distributed throughout the red cell. The author finds that in congenital syphilis, the hemoglobin decreases markedly in percentage and the reticulation is increased, especially in the second type. The increase in hemoglobin and the decrease in the rate of appearance of reticulated substances invariably result after a course of antispecific treatment, as may be evidenced by the Wassermann reaction becoming negative. Thus it may be concluded that the study of reticulated substances in the erythrocytes throws a considerable amount of light on the therapy and prognosis of congenital syphilis.

KATO, Los Angeles.

Internal Diseases

THE EMPLOYMENT OF LIVER FOR THE ANEMIA OF EARLY LIFE. J. P. CROZER GRIFFITH and J. P. SCOTT, M. J. & Rec. **128**:121 (Aug. 18) 1928.

From a summary of seven cases of anemia of different types and degrees, in only two did improvement follow the administration of liver. The seven cases are reported in the paper. The authors believe that there is no question that liver sometimes is of benefit to patients with anemia. Their experience, however, is that in the severe anemia of early childhood it may fail completely. When the condition permits of building up the hemoglobin through the administration of iron, it is probable that iron in any form will do good. Too great a dependence on this newer treatment will lead to disappointment. In these statements, reference is not made to pernicious anemia which is rare in early life.

DIAGNOSIS, MANAGEMENT AND TREATMENT OF PNEUMONIA IN CHILDREN. HARRY LOWENBURG, M. J. & Rec. **128**:126 (Aug. 18) 1928.

The author points out the two varieties of uncomplicated pneumonia, i. e., apical pneumonia and hilum pneumonia, both peculiar to infancy and childhood and both especially difficult of detection. These two types as well as subpleural pneumonia are discussed at length. Bronchopneumonia does not usually present serious difficulties; however, it is perhaps too frequently diagnosed. There is no specific treatment for pneumonia but rest. A flat abdomen and fresh air yield the best results. Sodium citrate in large doses combats acidosis toxemia and protects the kidneys, and sodium bromide may be useful. Empyema is the only complication mentioned in the article. The time and site of operation, the operative procedure and the postoperative treatment for this condition are discussed.

WILLIAMSON, New Orleans.

ESSENTIAL THROMBOPENIA. DEAN LEWIS, Northwest Med. **27**:261 (June) 1928.

The presence of thrombopenia in certain purpuras was observed in 1881. An associated phenomenon is the absence of clot retractility. It may result from faulty platelet formation or from excessive platelet destruction. The rapid increase in the number of platelets which follows splenectomy indicates that destruction is more important causully than is faulty thrombogenesis. Splenomegaly is noted in a number of cases of purpura. Lewis reports two cases of purpura in patients aged 3 and 8 years, respectively, both of whom were relieved of hemorrhagic phenomena and abnormal conditions of the blood after their spleens were removed.

ACUTE GLOMERULONEPHRITIS. C. H. HOFRICHTER, Northwest Med. **27**:382 (Aug.) 1928.

Acute and chronic infections, as well as arteriosclerosis causing arterial narrowing within the glomerulus result in ischemia of the blood flow in the efferent vessels surrounding the tubules. Obstruction to the venous outflow from the kidney produces albuminuria, hematuria and cylindruria, as demonstrated by Ivy. Acidosis in persons with diabetes causes the appearances of urinary changes simulating those of nephritis, but these disappear when the acidosis is corrected.

SCOTT, Philadelphia.

CASE OF HUMAN INFESTATION BY A DOG TAPEWORM. W. H. HOFFMAN, Porto Rico Rev. Pub. Health **4**:46 (July) 1928.

A fecal sample from a boy, aged 2 years, showed proglottids and uterine capsules of *Dipylidium caninum*, the common dog tapeworm. The child was in good health with no intestinal symptoms. The infestation would probably have remained undetected but for the mother's discovery of worm segments in the child's feces. One of the intermediate hosts of *D. caninum* is the dog flea. Infection of the dog results from his catching and eating fleas that harbor the cysticercoid forms of the worm. Presumably human infection takes place through a similar accidental ingestion. The child was known to have played so much with dogs that it was a matter of comment.

SANFORD, Chicago.

CHRONIC PURPURA IN A GIRL OF FOURTEEN YEARS. WILKIE, Tr. M.-Chir. Soc. Edinburgh M. J. **35**:159 (Aug.) 1928.

This communication concerns a girl of 14 years who had been a bleeder since early childhood. Hemorrhages had occurred from slight injuries or had arisen spontaneously over the body. When menstruation appeared, it caused alarming hemorrhages. The bleeding time was fourteen minutes, the coagulation time normal and the fragility of the red cells normal, but the application of a tourniquet caused petechiae. The platelets were as low as 18,000. After removal of the not greatly enlarged spleen, all symptoms disappeared.

NEFF, Kansas City.

NORMAL VENOUS PRESSURE IN CHILDREN. L. PAYAN, Comp. rend. Soc. de biol. **94**:344, 1926.

Determinations of the venous and arterial pressure were made on eighty-one normal children from 1 to 15 years old. Between the first and seventh years, the venous pressure is practically constant (from 6 to 7 cm. of water); after the seventh year it increases progressively, until in the fifteenth year it is 10 cm. The change is parallel with the change in maximum arterial pressure but not with pulse pressure.

KUGELMASS, New York.

A CASE OF ACUTE TOXIC-INFECTIOUS ICTERUS IN A BREAST-FED INFANT. WALTER PIAGGIO GARZON, La med. de los niños **29**:8 (Jan.) 1928.

An infant, aged 4 months, became suddenly ill with a yellow discoloration of the skin and the mucous membranes. The temperature rose to 38.8 C. (102 F.),

and the pulse was 165. The liver and spleen were not enlarged; the heart and lungs were normal, and there were no signs of hereditary syphilis. The urine was the color of mahogany and gave positive tests for bile salts. The blood showed 17,000 leukocytes and 6,080,000 erythrocytes, with 73 per cent lymphocytes. The serum contained bile pigments, and the bleeding and coagulation times were normal. Results of the Wassermann and Pirquet tests were negative. The symptoms disappeared after three weeks, but a mild secondary anemia resulted. The treatment consisted of administration of mild mercurous chloride and intramuscular injections of methenamine.

The author discusses the probable cause of this type of icterus and states that icterus is rare in late infancy and early childhood. Hemolytic icterus is ruled out because of the increased resistance of the erythrocytes. Because a gastro-intestinal disturbance preceded the attack of jaundice and because of elevation of temperature and leukocytosis, it is thought that the condition was brought about by a toxin or an infection originating in the intestine.

The author discusses the possibility of an infant with deficient hepatic function easily acquiring biliary infections from the intestinal tract and believes that a local hepatitis may follow a general infection.

DWYER, Kansas City.

INFECTIOUS ICTERUS. R. HECKER, Jahrb. f. Kinderh. **120**:114 (May) 1928.

Hecker reports a series of cases of infectious icterus occurring in a home for rachitic children in the vicinity of Munich. In one and three-quarters years, a series of fourteen cases were observed. Six children, aged from 2½ to 6 years, and eight adult caretakers were affected. The cases occurred in sequence, with a greater number during November. There were prodromal symptoms in the children, such as loss of appetite, vomiting and frequent anginas, and among the adults headache, malaise, vomiting and diarrhea which came on gradually with fever, icterus of the conjunctiva and bile in the urine. The fever lasted from one to four days. The course was benign in all cases. Bacterial investigations could not be made. Apparently Weil's disease was not a factor. The writer wonders what rôle the presence of numerous mosquitoes played at the time.

STENOSIS OF SPLENIC VEIN IN CHILDREN. G. WESTKOTT, Jahrb. f. Kinderh. **120**:232 (June) 1928.

Westkott reports the case of a girl, aged 10 years, who suddenly, without any prodromal manifestations, became ill with gastric hemorrhage evidenced by hematemesis and melena. While under medical care the patient developed a splenic tumor. On admission the child showed signs of severe anemia, was tired, but did not have any pain. Ascites was not present. There was a functional systolic blow over the heart. Retinal examination showed the remains of hemorrhage. Hematologic examination showed a severe secondary anemia with markedly lowered color index. A definite leukopenia developed. The resistance of the erythrocytes to saline solution was definitely diminished. Bleeding time was not increased. There was a concurrent infection with *Trichocephalus dispar*. Four days after a blood transfusion there was another hematemesis. Further changes in the size of the spleen did not occur. At the time the paper was written the anemia was cured, and no more hematemesis had occurred.

After considering in the differential diagnosis such conditions as ulcer, syphilis, tuberculosis, Hodgkin's disease, hemolytic anemia, Banti's disease and *Trichocephalus* intoxication, the author favors the diagnosis of stenosis of the splenic vein (Wallgren). Wallgren considers as characteristic for this disease (1) the combination of splenic tumor with hematemesis and (2) relationship between hemorrhage and size of the splenic tumor, in that during and after a hemorrhage the splenic tumor is smaller. Ascites may be present. The painful phenomena fluctuate and vary. Some patients complain of a feeling of heaviness in the splenic region; others complain of colicky pains; others do not have any pain.

The pathogenesis of the illness is explained by a hindrance to the flow of blood from the smallest venous sinuses to the opening into the portal vein. This condition may be brought about by compression from without, as occurs in congenital anomalies, gallstones, tumors, peritonitic adhesions or from inflammatory and sclerotic processes. The latter may be due to various causes, such as a purulent process in the navel, skin, bone marrow or pelvis. Wallgren thinks that every infection plays some rôle in this process. Thrombosis, organization and recanalization may occur and may extend into the portal vein. This leads to formation of a splenic tumor and a collateral circulation, by enlargement of veins in the phrenicocolic ligament or the gastrolienal ligament; and thus relationship to the esophageal or coronary veins is established. Varices form here, and these may cause serious hemorrhage.

The prognosis is serious, although the course of the illness is chronic. Fatality may occur from hemorrhage. The longest duration of the illness in a child was nine years. The chief therapeutic procedure is splenectomy with extirpation of the affected vein.

Blood transfusion shortly after hemorrhage is contraindicated here.

CHRONIC PYURIA. P. GYORGY, Jahrb. f. Kinderh. **120**:253 (July) 1928.

Gÿorgy writes that chronic pyuria is not an unusual clinical picture in childhood. In the recent literature there has been an increasing interest in malformations as a cause of chronic pyuria. Disturbances in the innervation of the bladder (as in spina bifida) have also been described. Among the malformations described are formation of valves in the posterior urethra, strictures, congenital megalo-ureter and accessory ureters. It is recommended that in every instance of chronic pyuria or subacute pyuria lasting eight or ten weeks a urologist be consulted.

The author reports five cases in children suffering from chronic pyuria on whom urologic examinations were performed, and the genito-urinary roentgenograms are reproduced. As the most frequent secondary manifestations, the author found ureteral insufficiency with dilatation and atony, either bilateral or unilateral. The right ureter was most often involved. The ureteral dysfunction eventually leads to functional disturbance of the kidney with resulting symptom of headache and hypertension, symptoms usually occurring in interstitial nephritis.

In conclusion, the author remarks that chronic pyuria is not a harmless condition and may lead to serious injury of the kidney.

METABOLIC INVESTIGATIONS IN HEPATIC CIRRHOSIS OF CHILDHOOD. HANS KNAUER and KURT FRIEDLANDER, Jahrb. f. Kinderh. **120**:292 (July) 1928.

Knauer and Friedlander write that cirrhotic disorders of the liver occur rarely in childhood. Cirrhosis tends to run a subacute course in children, in contrast to the chronic course in the adult. The duration is from several months to one year. Most of the cases observed occurred in children under 7 years of age. Males are more frequently affected than females. A sharp distinction between atrophic and hypertrophic forms is impossible in childhood. Half of the cases in childhood are associated with fever and hemorrhages. According to Seitz 33 per cent are due to acute infection, 16 per cent to chronic alcoholism and 15 per cent to syphilis. Some authors also mention toxic products from the gastro-intestinal tract as an etiologic factor.

In the pediatric literature there are a few references to metabolic disturbances in the hepatic cirrhoses: Bossert (*Monatschr. f. Kinderh.* **14**:174, 1918) reports glycosuria associated with a hypertrophic cirrhosis of the liver in an infant, aged 3 months. Warkany (*Ztschr. f. Kinderh.* **34**:305, 1927) found levulosuria in a child aged 3½ years, suffering from tuberculous cirrhosis of the liver associated with splenomegaly.

The author reports a case of hepatic cirrhosis in a girl, aged 4 years, with congenital syphilis. The Wassermann reaction was positive. The liver and spleen were palpable several fingerbreadths below the ribs. The child had several courses

of neoarsphenamine, bismuth compounds and mercury. At times there was a febrile reaction, and marked ascites developed early. There was a fatal termination of the illness. The autopsy showed lipoid nephrosis of the kidneys. The liver was small and showed evidence of interstitial hepatitis. The Levaditi stain for spirochetes was negative. The spleen was markedly enlarged and showed marked connective tissue perforation.

Study of the blood lipoids showed that the phosphatids fluctuated during the course of the illness from normal to above normal. Cholesterin was at first quite high and gradually came down to subnormal during the course of the illness. The free fatty acids showed slight changes. The bilirubin constantly increased during the course of the illness without reaching the stage of clinical icterus. A study of the carbohydrate metabolism showed diminished tolerance for levulose and galactose, a prolonged course of the blood sugar curve after ingestion of dextrose and an abnormally high rise and delayed return of the blood sugar curve after consumption of levulose. These disturbances are due to diminished ability of the liver to produce and fix the glycogen.

It is of interest to note that in spite of the severe disturbances in lipoid and carbohydrate metabolism the tetra-iodophenolphthalein test of Rosenthal was normal, showing again that a functional test may not give any information as to the total functioning of the organ.

ARTHUR ABT, Chicago.

CONGENITAL HEART DISEASE. H. RÖSLER, Wien. Arch. f. inn. Med. **15**:487, 1928.

In an exhaustive study, the author brings out many interesting observations. Among them, he points out that frequently in even pronounced cases of congenital heart disease, roentgen-ray examination will give entirely negative results. This was the case in more than 16 per cent of his material. He also finds that alcoholism and consanguinity are big factors in the etiology of congenital heart disease. He doubts very much if syphilis is an important factor or is of much influence as an etiologic factor.

SCHLUTZ, Minneapolis.

CONGENITAL STENOSIS OF THE PYLORUS. S. MONRAD, Acta paediat. **7**:16 (April) 1928.

Monrad's material covers 223 cases personally observed during a period of twenty-one years. His diagnostic criteria are the usual ones—projectile vomiting, usually appearing first before the end of the first week of life; vomiting; visible gastric peristalsis; gastric retention; malnutrition; oliguria and pseudo-obstipation. He has not excluded cases from his series for lack of a palpable tumor. Boys were affected three and a half times as often as girls. His gross mortality was 14.8 per cent, but if one excludes patients who were moribund when first seen, the figure falls to 4.5 per cent. Among the 190 who recovered, there were many with severe cases—68, in fact, who weighed less than 3,000 Gm. (6 pounds 4 ounces) when treatment was commenced. The author's interpretation of the pathogenesis of pyloris stenosis is that it is a congenital hypertrophy of the sphincter muscle, and he gives his evidence for this theory. Since all his patients are treated medically, it is of interest to note his data of the total duration of vomiting; one month in 58 patients, two months in 82 patients, three months in 30 patients and more than three months in 16 patients. The majority were put on breast milk, but good results were obtained also with butter-flour mixture, raw cow's milk and sterile milk mixtures. No advantage was gained from formulas low in fat. Thick feedings were of help only exceptionally. Small amounts of food were given at one time, ranging from 20 cc. every two hours to 150 cc. every three hours. Patients who vomited immediately after a feeding were refed. The stomach was emptied once or twice a day by tube, and in the majority of cases was washed out with physiologic sodium chloride solution. Fluids were given by rectum or subcutaneously. Patients showing subnormal temperature were treated in a steam tent. Medication formed a

minor part of the regimen, atropine being used in only thirteen patients, and with distinctly beneficial results in only three of these. In the author's opinion, medical is still preferable to surgical treatment.

THE PATHOGENESIS AND TREATMENT IN PYURIA. H. R. KROGSGAARD, Acta paediat. **7**:51 (April) 1928.

Krogsgaard briefly presents the results of study and treatment in 572 cases of pyuria.

The complete article is published elsewhere (he does not say where).

DIABETES MELLITUS IN CHILDHOOD. E. LENSTRUP, Acta paediat. **7**:130 (April) 1928.

Brief clinical reviews are given of four diabetic patients under 5 years of age, including one of 11 months. The guiding principle has been to look after the general welfare of these patients primarily, making glycosuria and hyperglycemia secondary considerations. Thus the prohibitions to which such patients are subjected are reduced to a minimum. When possible, the entire dose of insulin for one day is given in one injection. The hunger which young diabetic patients experience is usually a besetting thought, not amenable to distraction through amusement. On the other hand, minor influences will often give rise to a dyspepsia which leads to hypoglycemic symptoms through failure of absorption of the food. Such episodes appear to occur more frequently when the proportion of fat in the diet is abnormally high. Close observation of the blood sugar demonstrates the peculiar lability of the blood sugar regulating mechanism from which these patients suffer. Reactions from insulin are often seen and are as a rule easily controlled with treatment and do not leave any after-effect; yet they are occasionally of serious consequence. Synthalin was not effective in controlling the diabetes and gave rise to objectionable subjective symptoms. In the treatment for coma and precoma, milk may be offered without limit and has the double advantage of being welcome to the patient and of affording plenty of available carbohydrate during intensive administration of insulin. Minor infections are of the utmost import in their power to reverse the favorable progress of young patients.

ASCARIASIS IN AN INFANT OF ONE AND ONE-HALF YEARS. H. R. KROGSGAARD, Acta paediat. **7**:202 (April) 1928.

A persistent case of ascariasis, in which the worms were of unusual size and color, is presented.

CLINICAL AND ANATOMIC INVESTIGATIONS OF CELIAC DISEASE. C. E. BLOCH, Acta paediat. **7**:207 (April) 1928.

Bloch answers three questions pertaining to celiac disease. Does the infantilism have any connection with a deficient supply of vitamin? He thinks not. Is the tetany of intestinal infantilism identical with tetania infantilis? The behavior of the two is similar, and he believes that tetany in celiac disease is caused by the precipitation of calcium as soaps in the stools. What are the anatomic changes in the digestive organs? By injection of solution of formaldehyde into the stomach and peritoneal cavity shortly after death the usual postmortem changes were aborted, and the author found a subchronic inflammation of the mucous membranes of the stomach and intestine and a deficiency of granules in the secretory cells of the gastric glands.

PRESCORBUTIC MYOPATHY SIMULATING GROWING PAINS. C. FRIDERICHSEN, Acta Paediat. **7**:246 (April) 1928.

In older children, the prescorbutic state is often manifested by muscle tenderness, flaccidity and loss of tone (showing frequently as flat feet), and later by tonic contracture and by anorexia and fatigability.

BILIRUBIN STUDIES IN EPIDEMIC JAUNDICE. Z. ERIKSSON, Acta paediat. **7**:275 (April) 1928.

By means of Meulengracht's method for estimating the bilirubin content ("icteric index") of fluids, Eriksson studied blood serum and tissue fluid obtained from cantharides blisters during the course of epidemic jaundice. The index followed nearly the same sharply rising curve in both blood and vesicle fluid during the first few days of the disease. Commencement of improvement was announced by a sudden sharp drop in the blood bilirubin level, while the bilirubin curve of the vesicle fluid continued upward for some time before turning downward. Severe cases showed oscillations in both curves, and superimposed infections sometimes caused a temporary rise of bilirubin both in the blood and in vesicle fluid during convalescence. The duration of persistence of an elevated bilirubin index depended on the severity of the individual case.

McINTOSH, Baltimore.

CLINICAL OBSERVATIONS ON SERUM SICKNESS. SHIGENOBU KURIYAMA, J. Infect. Dis. (Tokyo) **2**:1015 (July 20) 1928.

Kuriyama finds that of 524 patients who received therapeutic serum for various conditions, 132, or 25.1 per cent, developed serum sickness. Most of the total number of patients were treated with diphtheria antitoxin (261). The incidence of serum sickness depends on the quantity and method of injection. In cases in which from 2 to 5 cc. of serum was injected there was no reaction, and as the quantity of serum increases, the incidence of reaction also increases. Of various methods of injection, the reaction occurs most frequently in cases of intravenous and intraspinal injection. As to the relation of age to serum reaction, the author finds that the older the patient the greater is the chance for reaction. The incubation period is usually six or seven days, and more than half of the reactions appear between five and nine days. In cases in which second injection is made, the incidence is greater. In nineteen cases showing serum reaction, the blood picture proved to be essentially that of leukopenia, with the relative increase of lymphocytes and consequent decrease of polymorphonuclear neutrophils, at the beginning of the reaction. As a means of prophylactic treatment, it is advised that efforts be directed toward perfecting a highly concentrated serum so as to minimize the dosage of single injections.

A CASE OF SUBACUTE LYMPHATIC LEUKEMIA WITH SUBCUTANEOUS NODULES. TSURUO KASAHARA, J. Pediat. (Tokyo), May, 1928, no. 336, p. 887.

The author reports a rare case of lymphatic leukemia with numerous subcutaneous nodules, especially marked on the face and scalp, in an infant, aged 1 year and 9 months. The most interesting lesion was seen on the scalp over the left parietal bone, which was about the size of an ordinary hen's egg, with irregular surface, an ulcer the size of a bean, an area of boardlike hardness with infiltration and reddish discoloration and an eminence of pale waxy consistency. The hair of the scalp was absent in these areas of nodular formation. There were other numerous reddish and brownish nodules, all about the size of the average lima bean. The color on the nodules did not disappear on pressure. These nodules were absent in other parts of the body.

KATO, Los Angeles.

Nervous Diseases

RECURRENT "ATTACKS" OTHER THAN MIGRANE AND INFANTILE CONVULSIONS PRECEDING "TRUE" EPILEPSY. D. M. LEVY and H. T. PATRICK, Arch. Neurol. & Psychiat. **20**:443 (July) 1928.

In the records of 500 private patients with "essential" epilepsy, sixty-four cases were found in which recurrent attacks, other than migrane or infantile convulsions, preceded the "true" seizure for periods varying from one week to about

forty years. A study of these attacks was made in an effort to determine the existence of "forerunners," or pre-epileptic seizures and, if possible, to enable their recognition and hence treatment at the most favorable time.

The classification by characteristics and related symptoms, including the number of cases in each group, was: group 1, attacks of "dizziness" and "fainting," seventeen cases; group 2, attacks of vomiting or belching and epigastric sensation, thirteen cases; group 3, attacks of hot flushes and pallor, three cases; group 4, sensory attacks in the face, head and body, three cases; group 5, attacks of throat spasm, asphyxia and thirst, three cases; group 6, attacks of screaming, crying and laughing, five cases; group 7, attacks of "dreamy states," "queer feelings," and change of consciousness, eleven cases; group 8, attacks of insomnia, drowsiness and night terrors, three cases; group 9, attacks of sudden disturbances of gait, three cases and group 10, attacks of "visions," "darkness" and "buzzing in the ears," three cases.

THE SYMPTOMATOLOGY OF TUMORS OF THE FRONTAL LOBE. P. E. KUBITSCHEK, Arch. Neurol. & Psychiat. **20**:559 (July) 1928.

In a study of twenty-two patients, two were under 20 years of age, the youngest was a boy of 7. The symptoms were classified as follows: Headache was present in twenty-one cases, vomiting in thirteen, failing vision in seventeen, convulsions in nine and mental disturbance in five cases.

SANFORD, Chicago.

BIRTH PARALYSIS. T. RUSSEL KUHN, M. J. & Rec. **127**:123 (April 1) 1928.

Birth paralysis may be peripheral, spinal or cerebral. The prognosis of the spinal and cerebral type is bad; that of the peripheral type depends on the amount of injury of the nerves involved. Deaths from cerebral hemorrhage may be greatly reduced by proper prophylactic measures such as: (1) prenatal care; (2) prevention of prolonged labor, and (3) proper management of obstetric manipulations as in the case of forceps. The best treatment for cerebral hemorrhage is absolute rest.

WILLIAMSON, New Orleans.

EPIDEMIC CEREBROSPINAL MENINGITIS. SOUREN TASHJIAN, Northwest Med. **27**:389 (Aug.) 1928.

Tashjian reports ten cases of meningococcus meningitis occurring in a rural community. Five were in men who had attended a lodge meeting; the wife and three children of another member of the lodge, and a girl who was treated by a dentist who had been at the meeting were also affected. The contact of the men at the meeting was close because of handshaking and wrestling matches. The dentist and the member whose family was affected both showed positive throat cultures. The epidemic was of a fulminating type, six of the patients dying shortly after the onset.

SCOTT, Philadelphia

JUVENILE TABES DORSALIS. C. WORSTER-DROUGHT and F. C. DANOERS-ATKINSON, Proc. Roy. Soc. Med. **21**:1254 (May) 1928.

The foregoing case was reported in a boy, aged 13 years. The report contains the results of a full examination of the central nervous system and of the cerebrospinal fluid.

WILLIAMSON, New Orleans.

THE PUPILLARY REFLEX IN INFANTS. M. NAKAOJI, M. KUHARA, S. INAMATSU and T. IMOTO, J. Pediat. (Tokyo), Aug. 20, 1928, no. 339, p. 1337.

Examining the pupillary reflex of 2,293 infants under 2 years of age, the authors find that during the first two months of life there is practically no reflex

of this kind, but that the boys manifest this reflex at 2 months, while in the girls it appears at 3 months. The rate of appearance increases rapidly in the fifth and sixth months, when it is present in 75 per cent of the girls and in 80 per cent of the boys. At 9 months, the boys show this reflex in nearly 100 per cent of the cases, while the girls show 100 per cent at 11 months. The pupillary reaction is a simple manifestation of stimulation of the afferent nerve (optical) and the response on the part of the efferent nerve (facial), and this forms a simple reflex arc. The authors disagree with Preyer, who believes the reaction to be a defensive movement.

KATO, Los Angeles.

Diseases of the Eye

THE FIGHT AGAINST TRACHOMA. EMIL GODLEWSKI, Opieka Nad Dzieckiem **6**:238, 1928.

Considerable trachoma exists among the children of Poland, particularly in those in asylums and orphanages. Conditions due to the World War undoubtedly favored the spread of the disease. The control of the disease must commence by examination of the children in the schools and orphanages. The first group living at home may be cared for in the dispensaries and ambulances. It is suggested that the group of orphans might better be cared for in large hospitals established in different centers for the express treatment of trachoma. To prevent further spread there should be a periodic examination of school children with elimination of all found to have trachoma, and better provisions for proper hygiene in the orphanages.

LESLIE, Evanston.

Diseases of the Ear, Nose and Throat

MASTOIDITIS AND OTHER FOCI OF INFECTION: A CAUSE OF GASTRO-INTESTINAL DISTURBANCE IN CHILDREN. MORRIS L. BRIDGEMAN, Northwest Med. **27**:332 (July) 1928.

Infants who do not thrive on a suitable adequate diet should be studied in relation to foci of infection. The common sites of focal infection in infants are the middle ear, mastoid, adenoids, sinuses, tonsils and renal pelves. As far back as 1898, the association of purulent otitis media and mastoiditis with fatal gastro-intestinal disorders was remarked on by pathologists at the necropsy table. Since 1921 a number of workers have performed antrotomy on these patients, with more or less gratifying results. Physical signs of mastoid infection may or may not be present. Often its detection is impossible except by antrotomy, which, however, is a simple process in infants. Bridgeman describes ten patients, on six of whom antrotomy was performed, four of whom recovered. Three cases of otitis responded to myringotomy, and one case of maxillary sinusitis responded to puncture and irrigation.

SUBMUCOUS RESECTION IN CHILDREN. R. E. WINDHAM, Northwest Med. **27**:392 (Aug.) 1928.

The great majority of writers on this subject do not favor submucous resection before the age of 16, largely from fear of subsequent deformity of the external part of the nose. Windham believes that many sinus diseases and other nasal disorders are allowed to affect the child's health because of this conservative attitude. He advocates more frequent operation and finds that deformities have not occurred in fifty-eight children so treated. His technic is to leave as large a piece of cartilage as possible anteriorly, with as deep a band as possible back to the attachment with the nasal bones.

SCOTT, Philadelphia.

PRIMARY TUBERCULOSIS OF THE MIDDLE EAR IN EARLY INFANCY. H. KLEINSCHMIDT and P. SCHURMANN, Monatschr. f. Kinderh. **40**:193, 1928.

Three cases are described in which the first symptom was a swelling near the ear. The ear started discharging usually from one to five weeks afterward. Then, characteristically but not infallibly, facial paralysis developed. The tuberculin reaction was, of course, positive. The disease is purely local and does not interfere with the growth of the child. Neither surgical nor x-ray treatment was effective. The tubercle bacilli were probably of the human type, and in some way gained direct access to the tympanic cavity.

GERSTLEY, Chicago.

OTITIS MEDIA IN INFANTS. FRANZ VON TORDAY, Ztschr. f. Kinderh. **44**:339 (Oct.) 1927.

It may be helpful to know that some authorities, like Czerny, never let an ear be punctured and that others require, before puncture, in addition to the bulging of the drum, indications in the general condition, such as restlessness. In other words, the appearance of the drum membrane is of secondary importance. Since paracentesis is not a life saving operation nor an emergency measure and should be performed to relieve signs of accumulated exudate or secondary symptoms, found especially in neuropathic infants, it has little justification when done only for exploration. The experience of von Torday, in 153 cases of otitis media, with 6 cases of mastoiditis, would seem to show that a difference does not exist in occurrence or degree of parenteral symptoms, in the degree or duration of suppuration, in the course of the disease or in the frequency of complication. To enable one to tell whether bone has been infected by a purulent inflammation from otitis media, studies in morphology are instructive; for example, a shift of less than 10 per cent to the left of Shilling's formula indicates that illness of an infant is not caused by an infection arising in the ear. The operation for mastoiditis is not borne well by infants, and conservative measures should be used, if possible.

OTITIS MEDIA IN INFANTS FROM THE HEMATOLOGICAL POINT OF VIEW. ZOLTAN V. ROKAY, Ztschr. f. Kinderh. **44**:347 (Oct.) 1927.

Infants in whom otitis media ran its course entirely without fever frequently showed high grade changes in the blood picture. In atrophic infants who did not have the capacity to react to otitis media with fever and in whom all the reactions of the organism in general were diminished to the minimum, a severe alteration of the blood picture often happened, as the only sign of a focus of pus present. Normally, less than a 10 per cent shift to the left in the blood picture of infants excluded the probability of a dangerous otitis media. In such cases, an explorative paracentesis was not indicated. In the differential diagnosis between influenza without complication and otitis media, a blood picture showing more than a 15 per cent shift to the left indicated otitis media. In a portion of the cases, especially when thick pus was found after paracentesis, there was a sudden improvement in the blood picture which had showed previously, in daily smears, a distinct shifting to the left. In these cases, the good results of paracentesis were to be capitalized. In another group of the cases, on the contrary, there was a rapid impairment to be seen in the daily blood picture after paracentesis. Many of these cases did not show pus immediately after the paracentesis; indeed some of them did not show otitis media. When impairment was demonstrable, in spite of free suppuration, one had to assume that the process had been generalized by the incision in the drum. Septic otitis may not be distinguished from severe otitis media by the qualitative blood picture. An intensive consideration of the blood, including the differential count, however, discloses a remarkable and characteristic picture hitherto undescribed in the literature, which makes possible in infants the immediate diagnosis of the septic nature of otitis media.

EMERSON. Boston.

TONSILLAR HYPERTROPHY IN SCHOOL CHILDREN. P. HERTZ, Acta paediat. **7**:97 (April) 1928.

Hertz followed 1,185 children over a period ranging from two to six years. He found that definite tonsillar hypertrophy may disappear spontaneously within a year, and that the presence of enlarged tonsils is not, on the whole, accompanied by a higher morbidity for infections.

McINTOSH, Baltimore.

Diseases of the Skin

RADIUM TREATMENT OF VASCULAR NEVI IN INFANTS. G. V. STRYKER, J. Missouri M. A. **25**:417, 1928.

The reason for treating a nevus or angioma is to remove a disfiguring and disturbing lesion or to prevent the possibility of hemorrhage. Cavernous angioma may heal spontaneously but leave bad scars. Various methods have been used. Excision is useful in covered parts. Electrolysis is the method of choice in spider nevi. Carbon dioxide snow is of value in some cases. The author believes, however, that treatment with radium surpasses all other methods. It is painless and, without infection, destroys the blood vessels of the nevus. Neither the x-ray nor radium, however, is to be used in the port wine nevi (nevus flammeus), the cells of which are fully developed at birth. For this type, carbon dioxide snow is best. The authors give a concise summary of the biologic and histologic characteristics of the cells and their reactions to the different rays in radium. The interval between treatments with radium should be four or six weeks. A treatment should not produce erythema.

SCHORER, Kansas City, Mo.

ATROPHIES AND SYNECHIAS OF THE NAILS OF HEREDITARY SYPHILITIC ORIGIN. P. RAVAUT and MONNEROT-DUMAINE, Ann. de dermat. et syph. **9**:461 (June) 1928.

The authors differentiate between syphilitic ungual dystrophy of congenital and of noncongenital origin. The latter is rare. They report a case in which deformations of the nails was first noted when the patient was 6 years old. There was a slow progression of the disorder. Varying grades of dystrophy of the nails were present. Longitudinal striation, atrophy and crumbling of the free border were the most prominent features. Not all of the nails were affected. The patient had a partially positive Wassermann reaction of the blood. Definite information concerning syphilis in the patient's antecedents is not reported.

LESIONS OF THE DUCTLESS GLANDS IN HEREDITARY SYPHILIS. J. PAYENNEVILLE and F. CAILLIAU, Ann. de dermat. et syph. **9**:469 (June) 1928.

The authors' investigation consisted in histologic and parasitologic study of the endocrine glands in children who died with manifest congenital syphilis. They detail four cases: three in which myxedema and one in which acromegaly were associated with congenital syphilis. Several other infants were studied, but in them the interpretation of the endocrinous symptoms was more difficult. As a result of their study, the authors state that in congenital syphilitic persons who present endocrinous disturbances, histologic examinations of the endocrine glands show the characteristic pathologic changes of syphilis and often the presence of *Spirochaeta pallida*. The lesions usually begin in the trabeculae of the connective tissue of the gland. These histologic changes are probably constant in congenital syphilis and it seems logical to deduce that these lesions are the basis for the clinical dystrophies of the congenital form of this disease. The authors think that it is probable that the same conditions often occur in acquired syphilis and explain the endocrinous symptoms frequently encountered in the acquired type.

CONGENITAL PALMAR ERYTHROKERATODERMA WITH POROKERATOSIS. GOUGEROT, J. MEYER and P. THIROLOIX, Bull. Soc. franç. de dermat. et syph. **35**:399 (May) 1928.

Associated with typical congenital palmar keratoderma were some isolated, conical, centrally depressed lesions suggesting porokeratosis.

MICHAEL, Houston, Texas.

THE MANAGEMENT OF FURUNCULOSIS IN INFANTS (STIMULATION AND VACCINE THERAPY). ZOLTÓN VON BÓKAY, Jahrb. f. Kinderh. **119**:240 (March) 1928.

In recent years there has been considerable improvement in the results of treatment for furunculosis in infants. Von Bókay mentioned various modes of stimulation therapy such as injections of the patient's own blood and injections of the mother's blood. Injection of milk is also mentioned as stimulation therapy. The author, however, was not completely satisfied with therapeutic results thus far and became more interested in the vaccine therapy of furunculosis.

He used commercial staphylococcus vaccine and also autovaccine. The dose of stock vaccine was 20, 50, 100, 200 and 500 million bacteria given by increasing doses every third day. The injections were given subcutaneously. Fifteen infants were treated; the furuncles began to disappear rapidly, and new ones did not arise. Fourteen of the children were cured in the comparatively short period of from two to three weeks.

The author describes his technic in preparing autovaccine. He concludes that vaccine therapy plays an important rôle in the treatment for furunculosis in infants. Concentrated vaccines are not recommended. The stock vaccine is recommended for general use and the autovaccine only in case the former is not effective.

Finally he mentions Besredka's antivirus which recently has been receiving favorable reports in the literature and with which he is working at present.

ARTHUR ABT, Chicago.

Surgery and Orthopedics

CARCINOMA OF THE OVARY IN INFANCY. V. C. HUNT, Ann. Surg. **77**:84, 1928.

This is a report of a carcinoma of the ovary weighing 1,000 Gm. in an infant, aged 17 months. There was marked precocious sexual development, corresponding to puberty.

N. ENZER.

SEPARATION OF THE EPIPHYSIS OF THE INTERNAL EPICONDYLE WITH REPORT OF CASES. H. D. SONNENSCHEIN, M. J. & Rec. **127**:298 (March 21) 1928.

A thorough knowledge of the normal roentgenologic appearance of the elbow joint is essential, as often the epiphyseal lines are diagnosed as fractures, while slight separations of the epiphyses are classed as normal. Separation of the epiphysis of the internal epicondyle should be suspected in all injuries to the elbow joint. This separation varies in amount and requires close examination and comparison with the uninjured elbow. Close cooperation between the surgeon and the roentgenologist is required. Roentgenograms of every injury (however trivial) to the elbow joint should be made together with pictures of the normal elbow. Recognition of this entity will allow early treatment which may prevent delay in healing. The condition may exist with other fractures of the elbow joint, but treatment instituted for the fracture will restore the separation to normal. The author reports four cases.

SUCCESSFUL HERNIOTOMY ON A PREMATURE INFANT. FREDERICK GRUNECH, M. J. & Rec. **128**:125 (Aug. 1) 1928.

Herniotomy was performed on an infant, aged 1½ months. Having been born in the seventh month of gestation, the child weighed 1½ pounds (680.4 Gm.).

The parents had noticed protrusion of the hernia ten days before, but had been able to reduce it until fourteen hours before admission to the hospital when the child began to vomit and action of the bowels ceased. The operation was performed without anesthesia the same evening. Sixteen days later the child was discharged, weighing 3 pounds (1,360.7 Gm.). The operative procedure and the postoperative treatment are described in the paper.

WILLIAMSON, New Orleans.

THE ABDOMINAL EMERGENCIES OF CHILDHOOD. A. H. SOUTHAM, Practitioner **120**:364 (June) 1928.

Except for rare congenital anomalies, the intra-abdominal lesions encountered in childhood are:

1. *Acute Appendicitis.*—Acute appendicitis is the most common abdominal emergency and is often difficult to diagnose. Mortality is highest between the ages of 5 and 15 years. The symptoms of the typical attack are easily recognized.

When the appendix occupies a position high up beneath the liver, acute inflammation of the organ may involve the peritoneum of the under surface of the diaphragm and cause symptoms simulating pneumonia. The high temperature and the pulse respiration ratio, however, are not present. Conversely, a basal pneumonia may simulate appendicitis, and a careful examination of the chest and absence of rigidity of the abdomen clear up the diagnosis.

When the appendix is in the pelvis, the symptoms are less marked. The history of onset and rectal examination will aid in clearing up the diagnosis.

Tabes mesenterica, acute lymphadenitis, pyelitis and cyclic vomiting are other conditions simulating acute appendicitis.

Treatment is surgical. The author cautions against the initial doses of castor oil so often given for "bilious attacks" in childhood.

2. *Pneumococcal Peritonitis.*—The primary type of pneumococcal peritonitis with peritoneal involvement is the first sign of the infection. This almost always occurs in girls of the poor class of from 5 to 7 years of age and is essentially associated with dirt and neglect. The onset is found as a pelvic infection with rapid spread to the general peritoneal cavity and marked septicemia. Diarrhea is often the first symptom, other early symptoms being suprapubic pain and painful urination.

The treatment is simple drainage of the abdominal cavity. McCartney and Fraser explain the peculiar incidence of the primary form in girls from 5 to 7 years by saying that the infection reaches the peritoneal cavity through the patient's vagina and fallopian tube, and it is also suggested that the change in the reaction of the vaginal secretion from alkaline to acid after the seventh year explains the incidence of the disease.

3. *Acute Intestinal Obstruction.*—When occurring under 2 years, acute intestinal obstruction is almost always from intussusception; after that obstruction occurs as the result of adhesions or involvement of a persistent Meckel's diverticulum. Children stand the effects of intestinal obstruction badly, and with increasing absorption of toxin collapse is soon manifest. Absolute constipation, abdominal pain and clear return of a turpentine enema without the passage of flatus are indications for laparotomy, and one should not wait for the classic signs of obstruction to appear.

4. *Intussusception.*—Intussusception occurs chiefly in children under 1 year of age. Symptoms are sudden, and periodic attacks of pain and screaming occur. The child lies quietly between attacks, and blood and mucus but not any fecal matter are passed by rectum. A tumor is felt in 75 per cent of the cases.

Early diagnosis and prompt surgical relief will avoid many fatal results. Other methods of reduction should never be attempted. Enlarged glands at the ileocecal angle are found almost constantly at operation. It is possible that this

predisposes in some way to the formation of an intussusception, and all cases are necessarily associated with a loose attachment of the ascending colon.

5. *Congenital Pyloric Stenosis.*—Congenital pyloric stenosis occurs commonly at the second to the fourth week of life. The symptoms are vomiting, the vomitus not containing any bile, constipation and wasting. Visible peristaltic waves are encountered, and the hypertrophied pylorus may often be palpated.

The author concludes by saying that the treatment is always surgical.

GELSTON, San Francisco.

THE TREATMENT OF PNEUMOCOCCUS EMPYEMA IN CHILDHOOD WITH OPTOCHINE. PHILIPP LEITNER, Jahrb. f. Kinderh. **119**:227 (March) 1928.

Leitner describes the early history of optochine in the treatment for pneumococcic inflammations and its introduction by Morgenroth. He gives credit to Gralka (*Monatschr. f. Kinderh.* **23**:280, 1922) for suggesting the method for the use of optochine in pneumococcic empyema in childhood. The author reports on the successful results of optochine therapy in eight cases of empyema due to the pneumococcus, without noting any toxic effects on the eye or the ear. He remarks on the high mortality when rib resection is performed on infants and children with empyema and on the improvement in mortality statistics when multiple aspiration is employed.

The results of irrigation treatment with optochine for pneumococcus empyema are most favorable during infancy, the most unfavorable period for the operative procedure. The author advises puncture and drainage of the empyema cavity and irrigation with 0.5 per cent optochine solution, leaving some optochine in the cavity. This should be done at three or four day intervals as soon as the diagnosis is established.

The author advises a dosage of 25 mg. per kilogram for young infants. One should be particularly careful in the proper antisepsis of the skin before operation.

The author concludes with the statement that the successful results obtained with this mode of therapy encourage the hope that this method will take the place of rib resection in the treatment for pneumococcus empyema of infants and small children.

ARTHUR ABT, Chicago.

MUNICIPAL ASYLUM FOR INFANTS AT BYDGOSZCZ, POLAND. DR. ANTONI NOWINSKI, Opieka Nad Dzieckiem **6**:223, 1928.

The establishment is given over to the care of abandoned infants under 2 years of age. During the last year, 108 infants have been cared for, 15 of whom were legitimate and 93, illegitimate. On entrance they were, for the most part, underweight and were suffering from some gastro-intestinal disturbance. The total motality was 26, 13 of the deaths being due to gastro-intestinal conditions. Institutional care is not ideal but under present conditions seems unavoidable. Well supervised placement in families is to be desired.

LESLIE, Evanston.

Miscellaneous

EUGENIC STERILIZATION IN CALIFORNIA: I. THE INSANE. PAUL POPENOE. J. Social Hyg. **13**:257 (May) 1927.

Popenoe presents an analysis of the personnel of the group sterilized, as to number, place of birth, race, subsequent history, length of stay in the state institution, age at operation, sex ratio and type of psychosis. About one patient in every twelve in the California state hospitals for mental diseases has been sterilized. Many of these still remain in the hospitals, the operation having been performed primarily for therapeutic purposes. Most of this group have dementia praecox. The operation is performed almost wholly on those whose psychoses are, by common consent, most highly dependent on inheritance.

II. The Feebleminded, J. Social Hyg. **13**:321 (June) 1927.

The group of these patients in institutions are those forming social problems primarily. They represent only a fraction of the mentally defective population. The average intelligence quotient of those sterilized was 60. Some epileptic patients of high mentality were included. Most of the group remain under state surveillance, even though nominally paroled.

(Study III of this series appeared in the Proceedings of the American Association for the Study of the Feebleminded. It deals with administrative problems.)

IV. Changes in Administration, J. Social Hyg. **13**:468 (Nov.) 1927.

Since the first of these legalized operations in 1910, the percentage of sterilization of inmates of hospitals for the insane has varied from year to year, due to current administrative policy. At present it is increasing, approaching one fifth of all admissions. More patients are being sterilized at the time of their first admission, soon after commitment. More single women are being sterilized. Most of the group are patients with dementia praecox and manic-depressive psychoses.

V. Economic and Social Status of the Sterilized Insane, J. Social Hyg. **14**:23 (Jan.) 1928.

A statistical study is presented. The statistics are incomplete, being based on 200 of 15,000 first admissions to California hospitals from 1921 to 1926, inclusive. The status of these patients is compared with that of Terman's series of parents of superior children. It is concluded that "as practiced in California, it (sterilization) has affected a class of individuals who would certainly produce few, if any, superior children, and who with equal certainty would produce many inferior children."

X. Attitude of Patients' Relatives Toward the Operation, J. Social Hyg. **14**:271 (May) 1928.

Although not legally required, consent was obtained from relatives prior to operation in about three fourths of the cases. In about a sixth of the patients operated on, relatives were not accessible. In less than 10 per cent, consent was not obtained. To determine the reaction to the operation, questionnaires were sent to various follow-up workers. Twenty-two replies were received, dealing with observations on 290 males and 1,900 females who had been sterilized for periods varying from one to fifteen years. Some familial friction had arisen in a few instances secondary to the status of the sterilized person, but in no instance could a serious result be ascribed definitely to the operation. The social workers who answered the questionnaire were unanimous in the belief that the law was working well in this respect.

XI. Attitudes of the Patients Toward the Operation, J. Social Hyg. **14**:280 (May) 1928.

At the time of the study, 3,730 patients had been sterilized. Questionnaires were sent to 821 of these, and 173 replies were returned. Of these, 132 were pleased, 19 displeased, and 22 noncommittal.

International Traffic in Women and Children. Ray H. Everett, J. Social Hyg. **13**:269 (May) 1927.

Everett presents a review of the activities of the League of Nations along these lines and of the committee appointed by it to deal with this problem. Members obtained contact with leaders of the international ring of traffickers and were able to gain first hand information from them and from their subsidiaries in many countries. All evidence was authenticated before its acceptance, and the original

documents are on file in the League's archives. The "middleman" and the legalized licensing of prostitutes were considered as two of the chief factors to be combated in the abolishment of this evil. In a later issue of this journal (**14**:65 [Feb.] 1928), Bascom Johnson furnishes a continuation of the report, dealing with a review of part II of the report of the League and its revision after comments were received from the governments concerned in the report.

BOYD, Iowa City.

BLOOD TRANSFUSION. WILLIAM C. SPEIDEL, Northwest Med. **27**:267 (June) 1928.

Speidel recounts the physiologic effects of transfusion. He believes that it should be more widely used in septicemia. He stresses the importance of cross agglutination tests. He considers whole blood better than citrated blood.

SCOTT, Philadelphia.

A NEW ULTRAVIOLET TRANSMITTING GLASS. H. P. HOOD, Science **64**:281, 1926.

The Corning Glassworks have produced a new glass. "The cost of producing the glass is somewhat above that of window glass, but is far below that of quartz." Its transmission for wave lengths of 290 mm., the extreme limit of the sun's rays through the atmosphere, is 86 per cent through a 2 mm. thickness (uncorrected for surface reflections.) Thus the glass is practically equal to clear fused quartz.

KUGELMASS, New York.

INFANTILE ALCOHOLISM. MONCORVO FILHO, La med. de los niños **29**:48, 1928.

In an article running through five numbers of this Journal, the evil effects of alcohol down through the ages are described. Reports from many countries are cited to show that alcohol contributes to poverty, crime and ill-health. The author believes that it is an important factor in the social and economic life of the people and that the offspring of alcoholic parents are prone to convulsions, epilepsy, degeneracy, rickets and a high infant mortality. Breast milk from alcoholic mothers is deleterious to the nursing infant.

Reports of the Chicago Juvenile Protective Association show a much higher infant mortality in the families of alcoholic persons. Since the advent of prohibition, there has been a decrease in the number of inmates of penitentiaries in the United States as well as admissions to hospitals because of alcoholism.

Aquired alcoholism in children of from 11 to 12 years of age is prevalent in some countries. Grave disorders of digestion, cardiorenal disease and evidence of senile arteriosclerosis have been reported in these children.

INTERNATIONAL MEASURES FOR THE PROTECTION OF INFANTS. MARTINEZ VARGAS, La med. de los niños **29**:65 (March) 1928.

This paper was written at the invitation of the colleagues of Professor Schlossmann of Germany on the occasion of his sixtieth birthday. The author praises the work of Pfaundler and Schlossmann whose textbook was published in Spanish and exerted a great influence on the development of pediatrics in that country. He describes the work of protection of child life from the sixteenth century and the many agencies established in European countries contributing to the welfare of the child.

DWYER, Kansas City.

A COMBINED PERCUSSION-AUSCULTATION TEST FOR ENLARGED BRONCHIAL GLANDS. H. KOWARSKI, Jahrb. f. Kinderh. **120**:336 (July) 1928.

After a brief discussion of various symptoms and signs attributed to enlarged bronchial glands, Kowarski describes his mode of physical examination for bronchial adenopathy. He finds that this procedure, as checked by roentgen-

ograms, is more accurate than D'Espine's sign. The stethoscope is placed between the crest of the scapula and the vertebral column. Then percussion with the finger is performed over the spinal column from the level of the tenth thoracic vertebra upward. In normal children, a clear tone is obtained up to the third thoracic vertebra. The stethoscope bell may be placed alternately on both sides of the spinal column to determine which side is more involved.

ARTHUR ABT, Chicago.

ARE FOOTPRINTS OF THE NEW-BORN A CERTAIN MEANS OF IDENTIFICATION? M. HENKEL, Zentralbl. f. Gynäk. **52**:548 (March 3) 1928.

Henkel confirms the conclusion of Khreninger-Guggenberg that foot prints of the same infant vary to such a degree that they cannot be used as a means of identification. Photographic illustrations are given.

BRAHDY, New York.

THE PREDOMINANCE OF DIATOMS IN THE ORIGIN OF COD LIVER OIL. K. WEJDLING, Acta paediat. **7**:259 (April) 1928.

Wejdling claims to have seen droplets of fat "activated" in the interior of diatoms by incident ultraviolet rays. This activation persists several hours after death of the diatom, during which time the latter may sink to the bottom of the ocean and become food for codfish. Hence, the antirachitic power of cod liver oil is beautifully linked with sunlight.

MCINTOSH, Baltimore.

THE DEFINITION, THE FIELD AND THE LIMITATIONS OF SOCIAL SERVICE. H. RADLINSKA, Opieka Nad Dzieckiem **6**:205, 1928.

Social service is said to be the amelioration of life by man united to God. Its scope embraces all growth — physical, moral and intellectual. It must be limited by a respect for individual liberty. Practically, it involves an appreciation of economic needs and a willingness to satisfy them.

THE WELFARE OF YOUNG PEOPLE WHO WORK. K. KORNILOWICZ, Opieka Nad Dzieckiem **6**:213, 1928.

Of the 85,000 working adolescents (aged from 14 to 17 years), only 8,000 are being further educated in continuation courses, and the work of only 5,000 is controlled by factory inspectors. Only a small portion can profit from clubs, settlements and the like. There is great need for libraries, clubs, recreation grounds and camps. Welfare centers for young people who work should include vocational and educational guidance, help in hygiene and training and inspection of work.

DIFFICULTY IN RAISING ORPHANS. W. SZUMAN, Opieka Nad Dziekiem **6**:214, 1928.

The difficulty in raising orphans is in the lack of home environment. Many children come to orphan asylums without any knowledge of a father or mother and some without any knowledge of a home. Great care must be exerted by the personnel of the asylum to see that these children are properly brought up, and with sufficient sympathy. Of seventy-five children entering a representative asylum during one year, seventeen, or 23 per cent, had good parents; the rest fifty-eight, or 77 per cent, had unsuitable parents or were illegitimate. Twenty-five per cent had never known father or mother or home. Eleven per cent were weakminded; 4 per cent were cripples. While there is adequate provision for the physical care of these children in Poland, more attention must be paid to their bringing up.

LESLIE, Evanston.

Society Transactions

THE ASSOCIATION OF AMERICAN TEACHERS OF THE DISEASES OF CHILDREN

Twenty-Second Annual Meeting, June 12, 1928

J. P. CROZER GRIFFITH, M.D., *President, in the Chair*

SIMPLICITY IN TEACHING PEDIATRICS. DR. J. P. CROZER GRIFFITH, Philadelphia.

In our efforts at fulness of discussion we tell our students too much, and they, in their ignorance and lack of experience as to what is of real importance, go away with misconceptions. There are several sources to be blamed for what I can but regard as an unfitness of many students for bedside work when the medical degree is given them. First is the graded course. When the student passes his examinations in chemistry, anatomy, physiology, pathology and the like, and has done his laboratory work, he is disposed to feel that he is through with these, and straightway proceeds to forget what he has been taught. There should be a greater correlation between these studies and their application to disease.

The second matter to be blamed is the excess of laboratory work and I do not, of course, refer to the ordinary examinations of the urine and the blood. I know that there are two sides to this question, and that by discussion it has been worn threadbare. I will, therefore, not enter into it extensively further than to say that I believe thoroughly in laboratory instructions, but I think that it is possible for the students to get too much, absolutely and especially relatively, compared with the time spent on the bedside study of disease.

Third, as I said, the teaching of pediatrics itself is to blame. The teacher is more or less interested in the study especially of difficult problems and unusual cases — those connected with metabolism, chemical elements of the blood, uncommon urinary secretions, bacterial flora of the intestines, immunology, experimental medicine, the psychology and chemistry of the cerebrospinal fluid and so forth. I do not doubt that many teachers would rather spend an hour demonstrating and discussing a case of such clinical subjects even as Friedreich's ataxia, hereditary spastic paraplegia, inflammation of Meckel's diverticulum and the like, than they would choose to give an equal time to the symptoms and treatment of bronchitis or some more ordinary ailment.

Simplicity in teaching undergraduates might also be extended to some degree to the teaching of graduates by means of medical literature. Unimportant or confusing things and much that could well be omitted are often enclosed in the textbooks.

THE EDUCATION OF THE DIABETIC CHILD. DR. ELLIOT P. JOSLIN, Boston.

The diabetic child at the onset of his disease is taller and usually heavier than the average child and is mentally more precocious. Intelligence is inborn in the diabetic child. At the age of 10 years, he acquires a knowledge of diabetes far more readily than the average diabetic person of 50 years. Diabetic children are underfed and overfed by a physician's fiat, often without rime or reason, because time is not taken to study the individual case and unearth the real needs. It is not so simple a matter to teach the diet today as it was in the Allen era. Then, the Benedict test showed instantly any slight error in diet, but now it is less apt to be a true indicator of what has been eaten, because of the presence of insulin and the larger meals, as moderate additions to the diet are often tolerated. The most important education for a diabetic child is his diabetic education, because

on that his life depends. No matter how devoted his parents, no matter whether wealth allows a nurse, nothing will take the place of a child's acquisition of the fundamentals of his disease, and how to combat them successfully.

THE IMPROVEMENT OF MEDICAL INSTRUCTION. DR. M. E. HAGGERTY, Minneapolis.

College instruction cannot be delayed until all teaching problems have been resolved by experimental methods, but a clear perception of an application of this criterion of student activity would go far to correct many of the cruder delinquencies of college teaching. If the teacher would only ask himself the question, "What happens to my students when I do this or that particular thing?" he would have assumed the initial attitude necessary to the good teacher, and would have accepted a necessary criterion for the valuation of instructional technics. In the eagerness to have students acquire the content of their courses of instruction, the facts and principles that are set before them, college teachers are prone to overlook the fact that forgetting is as normal a process of the mind as that of learning itself. One safeguard against forgetting is the practice of relearning and overlearning commonly employed by good teachers in all the fundamental processes of education.

There can be little effective study of college teaching and little intentional improvement in it until the present marking system is discarded, or supplemented with corrective devices that render it intelligible. I plead for research in teaching problems. It is as a supplement to that body of knowledge which individual experience has so fruitfully contributed. Science has something to offer to the art of teaching as truly as it proffers aid to the art of medical practice, even though as yet its offering is largely by way of methods of investigation rather than by the verified bodies of knowledge.

THE TRAINING OF THE TEACHER. DR. ISAAC A. ABT, Chicago.

A teacher must have a thorough knowledge of his subject, though not all great scholars are equally great teachers. He should have a clear mind with a well developed memory and, above all else, a gift of logical reasoning. Early in his life he should learn several languages other than his own. If in this preparation a medical student also acquires some general culture, he will become better fitted for the dignified position which he will come to occupy and will add to his own happiness and contentment in life, as culture will help him to broaden his outlook and make more pleasing his contact with his fellow men and his students.

A successful teacher must love his work and desire to impart knowledge, but one who is enthusiastic about his particular branch, especially in the classroom, clinic or hospital ward, inspires his students with a love for the subject and awakens in them a desire to learn and to study. The large amphitheater clinic seems to have had its day. I am not fully in accord with this. I still believe that a well conducted clinic given occasionally to a large group of students is an excellent mode of presenting clinical material and demonstrating methods of work. The present method of instruction favors the teaching of small groups in hospitals or clinics. Even here, the instructors should understand the needs of the student and should work with him closely.

The admonition of the professor of pedagogy to his students consists of a few general commandments: First, be yourself what you would have your students become. Second, learn to know the students and the subject. Third, secure attention through interest. Fourth, lead students to find out, to tell and to do for themselves.

ORIGIN AND EARLY YEARS OF THE ASSOCIATION OF AMERICAN TEACHERS OF THE DISEASES OF CHILDREN. DR. SAMUEL W. KELLEY, Cleveland.

The Association of American Teachers of Diseases of Children was founded in 1907. The idea took place in the mind of Dr. John C. Cook. Dr. Cook com-

municated this generative impulse to Dr. Cotton. They came to me for counsel, and I promised to think over the matter. Having done so, I advised them that in my opinion there was no need of a new pediatric society of any of the kinds already in existence, but that there was one field badly in need of cultivation which yet was practically untouched, namely, the teaching of pediatrics. The first meeting was held at Atlantic City on June 3, 1907. I was made president; Dr. Charles Douglas, vice president; Dr. John C. Cook, secretary, and Dr. George H. Cattermole, treasurer.

Dr. Kelley gave in detail a description of the early meetings and progress of the society.

Book Reviews

OPERATIVE SURGERY. By J. SHELTON HORSLEY, M.D., Attending Surgeon, St. Elizabeth's Hospital, Richmond, Va. Third edition. Price, $15. Pp. 876, with 756 illustrations. St. Louis: C. V. Mosby Company, 1928.

In this, his third edition of Operative Surgery, Dr. Horsley treats in a masterly, comprehensive and concise manner in one volume, the whole scope of general operative surgery. The subject matter is based on material drawn from his own experience fused with the experiences of most of the leaders in modern surgery. He has omitted much of the early history and evolution of various surgical methods as well as many of the lesser important modifications of many of the standard and recognized operative procedures, and instead emphasizes certain fundamental principles such as biologic, physiologic and pathologic, and with especial reference to their relationship to surgical lesions, a relationship hitherto treated only scantily in textbooks on modern surgery.

It is on the basis of this recognized relationship that his operative methods are selected, and they are therefore designed so that the mechanical aspect of any surgical procedure disturbs to a minimum the biologic and physiologic functions of the organism and at the same time lend the best physical approach for the removal of the surgical pathologic lesion.

There is, therefore, much common sense in his chapters dealing with the biologic and physiologic aspects of surgical lesions as well as in those devoted to surgical drainage, technic, instruments, as also in the chapters dealing with the subject of complications after operations such as infection, shock and hemorrhage.

The book is more than a technical guide or manual in surgery. Each anatomic system is taken up separately and systematically from the standpoint of pathology, indication for operation, type of operation, complications after operations and their treatment. In addition to these, and something unusual for a book of this kind are the frequent photomicrographs of surgical pathologic lesions. All of the illustrations purporting the anatomic dissections and the various steps in operations are excellent, and the brief explanation of each figure makes them clear and understandable. The subject matter is, as a whole, pleasant reading because of its clearness and conciseness and is most useful because of its practicability.

NUTRITIVE ALLERGIE IN DER PATHOGENESE INNERER ERKRANKUNGEN ALS NÄHRSCHADEN ERWACHSENER. By CARL FUNCK, M.D. Price, RM. 3. Pp. 63. Berlin: S. Karger, 1928.

The object of the book is to distinguish disorders occasioned by the diet from other disorders. Funck states, "the most certainly deadly poison most frequently used is the daily food stuffs." He believes that the basis of the so-called nutritive allergic conditions is the faulty absorption from the gastro-intestinal tract and damage to the liver, so that the partially digested material absorbed is not completely destroyed. He names many disorders which are traceable to the diet, in some cases using only therapeutic tests as proof.

Walker's systems of tests are used with Coca's extracts in testing for the etiology of hives, angioneurotic edema, migraine, enteritis, anaphylactica and hyperesthetic rhinitis. Arthritismus, cramps and inflammatory phenomena, some types of migraine and angiospasm (essential hypertension) are mentioned as nutritive in origin in some cases only.

The article is written in a long-winded type of German, marked by frequent, clumsy repetition, and the information obtained is not worth the effort of wading through the book.

DISEASES OF INFANTS AND CHILDREN. By H. D. CHAPIN and L. T. ROYSTER. Sixth edition. Price, $7.50. Pp 675, with 184 illustrations and 10 plates. New York: William Wood & Company, 1928.

This is the sixth edition of this standard textbook. Many of the articles have been elaborated and the chapters rewritten. This has brought the material up to the present date. Practically all the recent advances in pediatrics that have been worth while and advantageous have been incorporated in the present edition. It is rather remarkable that so much can be crowded into such a small space. It need not be feared, however, that the original purpose of the book has not been conserved. It is still as readable and as complete as the former editions. The printing is good, and the illustrations are clear and well chosen. This edition like its predecessors fulfils the requirements of the student and the practitioner for a complete and readable textbook in pediatrics.

DIE ERNÄHRUNG GESUNDER UND KRANKER KINDER. By E. NOBEL, C. PIRQUET and R. WAGNER. Second edition. Price, 12 RM. Pp. 159, with 78 charts and illustrations. Vienna: Julius Springer, 1928.

This book is a well prepared outline of theories of nutrition as applied in the University Clinic in Vienna. Part one contains a brief discussion of theories of nutrition, while part two deals with their practical application (*a*) to healthy babies, (*b*) to healthy older children and (*c*) to sick children; the last chapter contains feeding formulas, diet lists and recipes.

Pirquet's "Nem" system of feeding is described in detail. His ideas regarding food-tolerance in infants are discussed at some length. There are many case reports given to illustrate the practical aspects of nutrition.

Directory of Pediatric Societies

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SECTION ON DISEASES OF CHILDREN

Chairman: Dr. W. A. Mulherin, 753 Broad St., Augusta, Ga.
Secretary: Dr. C. A. Aldrich, 545 Lincoln Ave., Winnetka, Ill.
Place: Portland, Ore. Time: July 8-12, 1929.

AMERICAN PEDIATRIC SOCIETY

President: Dr. Henry L. K. Shaw, 142 Washington Ave., Albany, N. Y.
Secretary: Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.
Place: St. Louis. Time: 1929.

THE ASSOCIATION OF AMERICAN TEACHERS OF THE DISEASES OF CHILDREN

President: Dr. Paul W. Emerson, 86 Bay State Road, Boston.
Secretary: Dr. Ralph M. Tyson, 1527 Pine St., Philadelphia.
Place: Portland, Ore. Time: July 8-12, 1929.

AMERICAN CHILD HEALTH ASSOCIATION

President: Hon. Herbert Hoover, 370 Seventh Ave., New York.
Secretary: Dr. Philip Van Ingen, 370 Seventh Ave., New York.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. Thomas Crossan Clark, 51 Herkimer St., Hamilton, Ont.
Secretary-Treasurer: Dr. Frank H. Boone, 164 James St. S., Hamilton, Ont.

SECTIONAL

CENTRAL STATES PEDIATRIC SOCIETY

President: Dr. J. Gurney Taylor, 120 E. Wisconsin St., Milwaukee.
Secretary: Dr. A. H. Parmelee, 310 S. Michigan Ave., Chicago.
Place: Milwaukee. Time: October, 1929.

SECTION ON PEDIATRICS OF SOUTHERN MEDICAL ASSOCIATION

Chairman: Dr. E. C. Mitchell, 1073 Madison Ave., Memphis, Tenn.
Secretary: Dr. A. J. Waring, De Renne Apts., Savannah, Ga.
Place: Asheville, N. C. Time: November 12-15, 1928.

LOCAL

NORTHERN CALIFORNIA PEDIATRIC SOCIETY

President: Dr. W. L. Channell, Medical Bldg., Oakland, Calif.
Secretary: Dr. J. E. Parrott, Medico-Dental Bldg., San Francisco.
Place: Various Teaching Schools. Time: Monthly.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. George P. Laton, 1136 W. 6th St., Los Angeles.
Secretary: Dr. William Sidney Bowers, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

THE ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. W. Wiley Jones, Majestic Bldg., Denver.
Secretary: Dr. Berryman Green, Republic Bldg., Denver.
Place: Children's Hospital, Denver. Time: Third Saturday of each month, 2:30 p. m., September to May, inclusive.

GEORGIA PEDIATRIC SOCIETY

President: W. N. Adkins, Medical Arts Bldg., Atlanta.
Secretary and Treasurer: Dr. E. N. Gleaton, 212 E. Gaston St., Savannah.

PEDIATRIC SECTION OF FULTON COUNTY MEDICAL SOCIETY, ATLANTA, GA.

Chairman: Dr. Willis Ragan, Medical Arts Bldg., Atlanta.
Secretary: Dr. Lee Bivings, Exchange Bldg., Atlanta.
Place: Academy of Medicine, 32 Howard St., Atlanta. Time: Second Thursday of each month from October to April, at 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

Chairman: Dr. William W. Howell, 279 Clarendon St., Boston.
Secretary: Dr. Randolph K. Byers, 66 Commonwealth Ave., Boston.
Place: Boston Medical Library. Time: Second Friday of each month.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Maurice Blatt, 185 N. Wabash Ave., Chicago.
Secretary: Dr. J. K. Calvin, 104 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. L. R. De Buys, 1417 Delachaise St., New Orleans.
Secretary-Treasurer: Dr. C. T. Williams, 7401 Burthe St., New Orleans.

DETROIT PEDIATRIC SOCIETY

President: Dr. M. Boyd Kay, 10 Peterboro St., Detroit.
Secretary: Dr. Charles A. Wilson, 71 E. Ferry St., Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. Ray Shannon, Lowry Bldg., St. Paul.
Secretary: Dr. E. S. Platou, 730 La Salle Bldg., Minneapolis.
Place: University Campus and Rochester. Time: Winter, Spring, Summer, Fall.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. Park J. White, Beaumont Bldg., St. Louis.
Secretary-Treasurer: Dr. Ralph L. Cook, 508 N. Grand Blvd., St. Louis.
Place: St. Louis Children's Hospital. Time: At least once a year and contingent thereafter on the arrangement of a suitable program.

NEBRASKA-IOWA PEDIATRIC SOCIETY

President: Dr. Floyd Clarke, City Nat'l Bank Bldg., Omaha.
Secretary: Dr. R. B. Eldredge, Medical Arts Bldg., Omaha.
Place: Add-Sell Restaurant. Time: Second Thursday of each month from October to May, inclusive, 6 p. m.

BROOKLYN PEDIATRIC SOCIETY

President: Dr. Louis M. Ruderman, 961 Eastern Parkway, Brooklyn.
Secretary: Dr. Joseph F. Paulonis, 1357 Bushwick Ave., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

BRONX PEDIATRIC SOCIETY

President: Dr. William Hinz, 1964 Grand Concourse, New York.
Secretary: Dr. L. H. Barenberg, 1749 Grand Concourse, New York.
Place: Concourse Plaza, 161st St. and Grand Concourse, New York.
Time: Second Wednesday of each month, except June, July, August and September.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various Cities in New York. Time: Fourth Thursday of October, January and April.

PEDIATRIC SECTION OF THE NEW YORK ACADEMY OF MEDICINE

President: Dr. Stafford McLean, 17 East 71st St., New York.
Secretary: Dr. F. Elmer Johnson, 300 West End Ave., New York.
Place: New York Academy of Medicine, 2 East 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

ROCHESTER PEDIATRIC SOCIETY

President: Dr. Paul W. Beaven, 26 S. Goodman St., Rochester, N. Y.
Secretary: Dr. Edwin R. Reynolds, 1620 St. Paul St., Rochester, N. Y.
Place: Arranged by Program Committee. Time: First Friday of each month from October to May.

THE PEDIATRIC SECTION OF THE ACADEMY OF MEDICINE OF CLEVELAND

Chairman: Dr. J. W. Epstein, 3912 Prospect Ave., Cleveland.
Secretary: Dr. Charles W. Burhans, 14805 Detroit Ave., Lakewood, O.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. Edward L. Bauer, Jefferson Medical College, Philadelphia.
Secretary: Dr. John Porter Scott, 2040 Pine St., Philadelphia.
Place: College of Physicians, 19 S. 22nd St., Philadelphia. Time: Second Tuesday of each month from October to June, inclusive.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. Zaccheus R. Scott, Westinghouse Bldg., Pittsburgh.
Secretary: Dr. Theodore C. Elterich, Highland Bldg., Pittsburgh.
Place: Pittsburgh Acadamy of Medicine. Time: Second Friday, alternate months.

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Secretary: Dr. Gilbert J. Levy, 899 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

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Secretary: Dr. W. Ambrose McGee, West End Medical Bldg., 2618 Grove Ave., Richmond, Va.
Place: Westmoreland Club, 601 E. Grace St., Richmond, Va.
Time: First Thursday of each month (other than during the summer).

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Place: College Club. Time: Third Friday of each month, at 7 p. m.

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Place: Children's Hospital, Milwaukee. Time: Second Wednesday of each alternate month, beginning with February.

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Secretary: Dr. G. A. Davis, 12 Belsize Dr., Toronto.
Time: November 17, December 15, February 16 and March 15.

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